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INDIAN JOURNAL OF MALARIOLOGY.

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THE INDIAN COUNCIL OF MEDICAL RESEARCH.

Editor:—Lieut Colonel JASWANT SINGH MB ChB DPH, DTM & H,
Director Malaria Institute of India, Delhi



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Tables, charts, etc., should be numbered, and alluded to in the text as 'Table I', etc., and not as 'the following table', etc.

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The following contractions are in use in the *Indian Journal of Malariology*, whether the number to be expressed is one or more —

gramme, gm, kilogramme, kg, centigramme, cg, milligramme, mg, metre, m, kilometre, km, centimetre, cm, millimetre, mm, cubic centimetre, cc, cubic millimetre, c mm, cubic foot, c ft

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Where degrees of temperature are given, the scale used should always be specified, e.g. 37°C, 98°F

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CHRISTOPHERS S R (1915) The spleen rate and other splenic indices *Ind J Med Res*, 2, 4, pp 823-866

The title may be omitted but the reference should always give author's name, year, abbreviated

..... y type
..... year
..... case,

The following are some of the abbreviations in use —

<i>Ann J Hyg</i>	<i>Ind J Mal</i>	<i>Rev App Ent</i>
<i>Ann Trop Med Parasit</i>	<i>Ind J Med Res</i>	<i>Rev Malariol</i>
<i>Brit Med J</i>	<i>J Mal Inst Ind</i>	<i>Trans Roy Soc Trop Med Hyg</i>
<i>Bull Ent Res</i>	<i>Jl R A M C</i>	<i>Trop Du Bull</i>
<i>Bull Soc Path Exot</i>	<i>J Trop Med Hyg</i>	<i>U.S.A Pub Hlth Rpts</i>
<i>C. R Soc Biol</i>	<i>Med Vet Ind Ind</i>	
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The *Indian Journal of Malariology* is published four times a year, in March, June, September and December. Each volume consists of four numbers.

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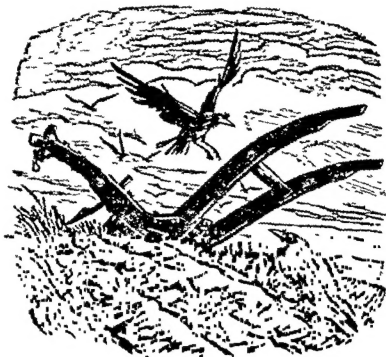
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PLATE III



B gader J A SINTON v c OBE MS (Retd)
Ed tor 19 J 1935

EDITORIAL

THE *Indian Journal of Malariology* has successfully completed 25 years of its service to the malaria world. Starting as *Records of the Malaria Survey of India*, its nomenclature was changed to *Journal of the Malaria Institute of India* in 1938 and finally switched over to *Indian Journal of Malariology* in 1947.

So far 22 volumes, each consisting of four issues, have appeared. It is a quarterly publication but in 1932-1933 and during the war years (1941-1946), when there was paucity of material for publication, one volume was completed in two years. For the same reason, two issues were combined into one, four times during the entire period. The total number of printed pages run to 11,506, average 523 pages per volume. During this period, 805 articles have appeared, average 37 per volume (Table I).

TABLE I.
Number of articles and pages published

Volume	Year	Number of articles	Number of pages
Records of the Malaria Survey of India			
1	1929-30	33	771
2	1931	25	664
3	1932-33	39	856
4	1934	24	428
5	1935	32	524
6	1936	33	676
7	1937	21	572
Journal of the Malaria Institute of India			
1	1938	39	440
2	1939	36	463
3	1940	44	619
4	1941-42	43	612
5	1943-44	37	477
6	1945-46	42	513
Indian Journal of Malariology			
1	1947	41	517
2	1948	19	327
3	1949	35	426
4	1950	41	506
5	1951	24	604
6	1952	43	540
7	1953	50	592
8	1954	50	593
9	1955	41	402
Total		805	11 506
Average per volume		37	523

Articles published are not only accounts of work done by the staff of the Malaria Institute of India (formerly Malaria Survey of India) and other Indian workers, but the journal has enjoyed the confidence of eminent research workers in foreign countries as well and includes as many as 58 contributions from them as per following details —

		746
India	9	
Africa	1	
Belgium	1	
Burma	12	
Ceylon	6	
Formosa	3	
France	1	
Holland	4	
Indonesia	1	
Ireland	2	
Italy	1	
Malaya	1	
Nepal	2	
Pakistan	1	
Palestine	1	
Switzerland	8	
U K	4	58
U S A	58	804

So far, 28 abstracts of articles of local importance (the original MSS having been kept in the library of the Malaria Institute of India for reference by workers who wish to consult them) and nine obituaries of eminent workers who left a wide gap among the malariologists of the world, have appeared in the journal. Review of important books has only recently been started and so far only four reviews have appeared.

The total number of authors who have contributed to the journal from time to time is 365. The largest number of pages contributed by a single author so far is 1,057 in 43 articles by Major General Sir Gordon Covell (Director, Malaria Institute of India from 1936 to 1947) and the largest number of contributions by a single author is 83 comprising 759 pages by Lt-Colonel Jaswant Singh (Director, Malaria Institute of India from 1947 to date).

The subjects covered include malaria in all its aspects (human, avian, simian and recently rodent—physiology of malaria parasite, pathology, chemotherapy, immunology, epidemiology and control), studies on mosquitoes, both *Culex* and *Anopheles* (distribution, vectorial capacity, relation to malaria, destruction by the use of insecticides, resistance to insecticides), blackwater fever, kala azar, filariasis, etc.

The Director, Malaria Institute of India, has been the ex officio editor of the journal. Brigadier J. A. Sinton remained the editor from 1929 to 1935 and

PLATE IV



MAJOR GENERAL CORBIN COVILLE U.S. ARMY
1936-1916

was assisted at times by Lt-Colonel H W Mulligan during 1935. Major General Sir Gordon Covell took up the editorship in 1936 and continued till 1946. He was assisted by Lt-Colonel M K Afridi up to 1939 and by Lt-Colonel Jaswant Singh from 1941 onwards. Lt-Colonel Jaswant Singh became the editor in 1947 and is still continuing.

The journal is financed by the Indian Council of Medical Research and besides money realized from sales, advertisements, etc., receives an annual grant of Rs 12,500 per year for its publication only.

It has a world wide circulation and has a special place among the malaria publications. There are at present 70 foreign and 98 Indian subscribers. Besides 114 copies issued in exchange, 112 copies are distributed free to eminent workers and institutions both in India and abroad. A large number of journals of international repute are received in exchange of this journal, which considerably augment the resources of the library at the Malaria Institute of India.

With the formation of Malaria Survey of India in 1927, it was felt necessary to dig out the old reports and articles relating to malaria all over the country. Some of these were included in provincial publications and many were still in the MS form. In the course of a three month tour throughout India, Sinton

India in 1929. In the second number, many which had appeared during previous years but were no longer available for general use, were reprinted.

There have been outstanding contributions by workers in India, viz., malaria in Sind by Sinton, Covell, and Bailly, treatment with cinchona alkaloids and what may be called the "Malaria Survey of India" contributions.

Barraud, Cove

Iyengar, Muirhead-Thomson, Pal and others, monkey malaria and extensive

Wats, Jaswant Singh,

Wats, Paul Russell,

and others, malaria

and its engineering aspects by Jaswant Singh, Henderson and others, studies on

Plasmodium berghei by Ramakrishnan, Satya Prakash, Krishnaswami and colleagues,

progress of antimalaria operations in Delhi by Covell, Afridi and Jaswant Singh,

in Bombay by Viswanathan, Ramachandrea Rao and colleagues, in Mysore by

Sweet, Rao and others, on B N Railway by Senior White and co-workers.

The study of malaria and its vectors in Borneo by McArthur and Colless,

studies on the bionomics of *Aquasalis* and its relation to malaria in British West

Indies by Senior White, malaria in Formosa by Watson and colleagues, are some

of the other notable contributions. Besides, special issues have been published

from time to time on Paludrine, Insecticides, Pyrimethamine, Malaria in Ceylon,

and a written symposium on *Plasmodium berghei* in which workers from all over the

world participated.

The journal has been one of the most important organs of the East (perhaps the only one of its kind) for making known the trend of malaria research and control. It has tried to help in the fulfilment of two of the main functions of the Malaria Institute of India (1) "To publish scientific results, useful guides, bulletins, etc.", and (2) "To keep alive interest in malaria study and prevention and to see that such interest, wherever present, is nursed and assisted". If India has launched upon the most gigantic programme of malaria control, it is because the malaria prevalence and its effects on the economy of the country, and in this the *Indian Journal of Malarology* has played a very prominent part. It has kept up its standard through many hazards it had to face during the war years.

The Jubilee Issue gives useful important reviews of the past researches and studies by eminent workers, and suggestions for the future on different aspects of the subject. It also depicts the present position of malaria control and research and paves a way for future programmes. It is a useful guide and a source of inspiration for those entering the field.

Recently the activities of the Malaria Institute have expanded to include some of the other communicable diseases, and the Malaria Advisory Committee of the Indian Council of Medical Research has also been redesignated as "Malaria and other Arthropod-borne Diseases Sub Committee" of the Communicable Diseases Advisory Committee. Whether the *Indian Journal of Malarology* should also widen its scope and welcome in its fold valuable knowledge about other arthropod-borne diseases and thus change its name once again, is a problem which will have to be considered in the near future.

This period of 25 years has been of great interest not only for contributors and readers but also for those connected with editing of this publication. Its future will no doubt be watched with interest.

The editor solicits the cooperation and patronage of contributors, institutions engaged in research and control of arthropod-borne diseases and also of those who are interested in emancipating the world of the misery caused by many preventable diseases.

PLATE V



FIG. 1. TAWANE IN H
No. 1. 11. 11
1. 1. 1. 1.

DO ALL THE HUMAN MALARIA PARASITES BELONG TO ONE GENUS?

As discussed by Christophers and Sinton (1938), Grassi and Feletti in 1890 divided the malaria parasites into two genera—first, *Hemamæba* to include the

mere differences in the form of the gametocytes was sufficient to justify the erection of two separate genera. He grouped all these parasites in the genus *Plasmodium* Marchiafava. This ruling has been followed by most workers from that time.

Since the discovery of the exo erythrocytic cycle of schizogony in malaria parasites, this problem needs reconsideration. The latest classification of this type of schizogony, as given by the World Health Organization's Drafting Committee on "Malaria Terminology" (Covell, Russell and Swellengrebel, 1953), shows that of the human species of *Plasmodium* s.s. as quite different from that of *Laverania*.

Now that the exoerythrocytic cycles of schizogony has been found to differ greatly in these two groups, does not this suggest that the classification given by Grassi and Feletti is justified? Should the genus *Laverania* be officially recognized as the correct name for such parasites as *Plasmodium falciparum* [vel *L. malariae* (Laveran)]

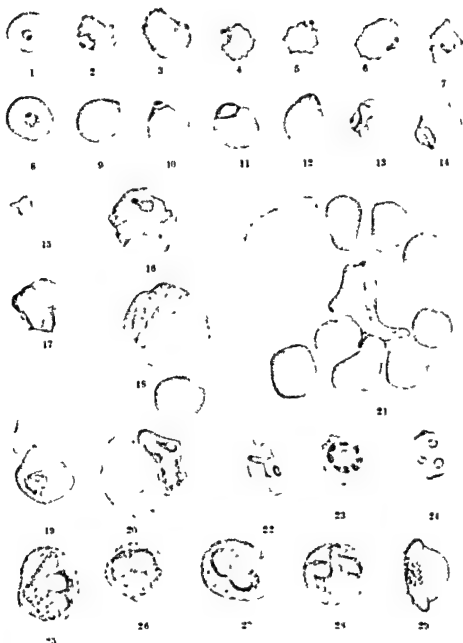
IS THE MALARIA PARASITE INSIDE OR OUTSIDE THE ERYTHROCYTE?

Laveran in his original description of the malaria parasites believed these to be extraglobular. Most of the other older writers like Marchiafava and Bignami (1894) asserted that they were within the red blood cells. Mannaberg (1894), however, thought that the young rings of the æstivo autumnal parasites were outside the erythrocyte.

Maurer (1902), in his paper on the stippling of red cells infected with plasmodia, came to the conclusion that the large and small ring forms of the pernicious parasite remained extracellular while they were in the peripheral blood. At the stage of development, however, when they disappeared into the internal organs, they entered the red cells.

The description given by Schaudinn (1902) of the entry of the sporozoite and the merozoite into the erythrocyte seemed to settle their intracellular position definitely. Rowley-Lawson (1914, 1918) again raised the question and produced evidence which cast doubt on the above finding.

The question was re opened by Sinton (1922). He pointed out that, on account of the very thin flattened shape of the erythrocyte, it was impossible by microscopical examination to ascertain whether the parasite lay in or on the cell (Plate VI, Fig. 1 and 8). He subjected the infested cells to hypertonic and hypotonic conditions to change their shape from a flat to a globular form. In *falciparum* infections this caused a great increase in the number of accolé forms



Figs. 1 and 2. *Leishmania tropica* (P. P. Chatterjee)

Figs. 3-5.

Figs. 6-13.

Figs. 14-17.

Figs. 18-21.

Figs. 22.

Figs. 23.

Figs. 24.

Leishmania tropica (P. P. Chatterjee)

DO ALL THE HUMAN MALARIA PARASITES BELONG TO ONE GENUS?

As discussed by Christophers and Sinton (1938), Grassi and Feletti in 1890 divided the malaria parasites into two genera—first, *Hemamaba* to include the quartan and benign tertian parasites, and second, *Laterania* to include those parasites which produced crescentic gametocytes. This classification was later rejected by Schaudinn (1902), who, from comparison with the *Coccidia*, did not consider that mere differences in the form of the gametocytes was sufficient to justify the erection of two separate genera. He grouped all these parasites in the genus *Plasmodium*. Marchiafava. This ruling has been followed by most workers from that time.

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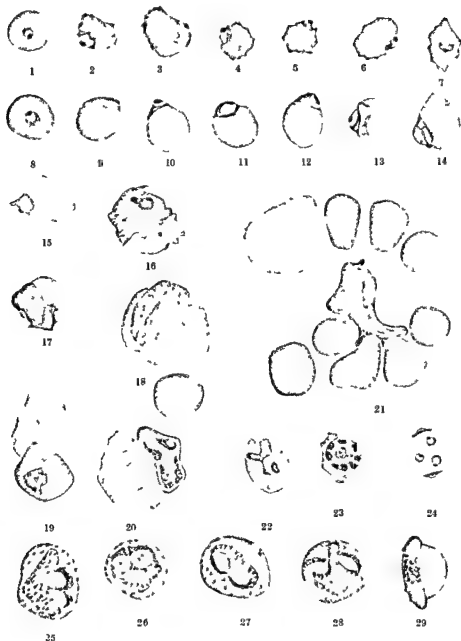
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Figs 1 and 8

Figs 2-7

Figs 9-17

Figs 18-20

Figs 21-24

Figs 25-29

Figs 30-34

Figs 35-39

Figs 40-44

Figs 45-49

Figs 50-54

P. falciparum with Maurer's dots in parasitised erythrocyte
 Mature schizont of *P. falciparum*
 Erythrocyte infested with multiple rings of *P. falciparum*
 Early stages of division of *P. malarie* schizont
 Gametocyte of *P. falciparum* with red cell "bib"

DO ALL THE HUMAN MALARIA PARASITES BELONG TO ONE GENUS?

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Marchiafava This ruling has been followed by most workers from that time

Since the discovery of the exo erythrocytic cycle of schizogony in malaria parasites, this problem needs reconsideration. The latest classification of this type of schizogony, as given by the World Health Organization's Drafting Committee on "Malaria Terminology" (Covell, Russell and Swellengrebel, 1953), shows that of the human species of *Plasmodium* s.s. as quite different from that of *Laverania*.

Now that the exoerythrocytic cycles of schizogony has been found to differ greatly in these two groups, does not this suggest that the classification given by Grassi and Feletti is justified? Should the genus *Laverania* be officially recognized as the correct name for such parasites as *Plasmodium falciparum* [vel *L. malarii* (Laveran)]?

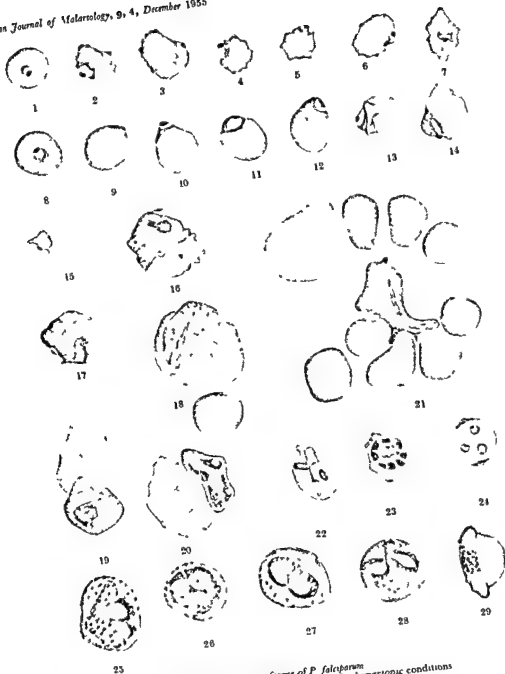
IS THE MALARIA PARASITE INSIDE OR OUTSIDE THE ERYTHROCYTE?

Laveran in his original description of the malaria parasites believed these to be extraglobular. Most of the other older writers like Marchiafava and Bignami (1894) asserted that they were within the red blood cells. Mannaberg (1894), however, thought that the young rings of the asexual autumnal parasites were outside the erythrocyte.

Maurer (1902), in his paper on the stippling of red cells infected with plasmodia, came to the conclusion that the large and small ring forms of the pernicious parasite remained extracellular while they were in the peripheral blood. At the stage of development, however, when they disappeared into the internal organs, they entered the red cells.

The description given by Schaudinn (1902) of the entry of the sporozoite and the merozoite into the erythrocyte seemed to settle their intracellular position definitely. Rowley Lawson (1914, 1918) again raised the question and produced evidence which cast doubt on the above finding.

The question was reopened by Sinton (1922). He pointed out that, on account of the very thin flattened shape of the erythrocyte, it was impossible by microscopical examination to ascertain whether the parasite lay in or on the cell (Plate VI, Fig. 1 and 8). He subjected the infested cells to hypertonic and hypotonic conditions to change their shape from a flat to a globular form. In *falciparum* infections this caused a great increase in the number of accolé forms



- FIGS 1 and 8 Erythrocytes with ring forms of *P. falciparum*
 FIGS 2, 7, 9, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, and 29 Acellate forms of *P. falciparum* produced by hypertonic conditions
 FIGS 3, 4, 5, 6, 10, 11, 12, 13, 14, and 20 Extracellular forms of *P. vivax* produced by hypotonic conditions
 FIG 21 Extracellular forms of *P. vivax* from moist chamber preparations
 FIG 22 *P. vivax* in grating from its host cell under moist chamber conditions
 FIG 23 Mature schizont of *P. falciparum*
 FIG 24 Erythrocyte infested with multiple rings of *P. falciparum*
 FIG 25 Early stages of division of *P. m. sch.*
 FIG 26 Merozoite of *P. falciparum* with red.

Erythrocytes carrying multiple infections, even as many as six, are not rare in severe malignant tertian infections (Plate VI, Fig 24). On the other hand, it is very rare to find even double infections with mature parasites of this species apart from any question of triple or quadruple ones. What happens to the other parasites? Are they swept off the outside of the host cell and perish, or do they then acquire fresh host cells as suggested by Rowley Lawson (1914, 1918)? It may be, of course, that so heavily burdened erythrocytes never emerge again into the peripheral blood from the internal organs, so escaping detection.

While the extracellular position of the parasites may help to explain some problems, yet it is difficult to understand the position of mature parasites in double infections such as were mistaken by Schaudinn (1902) for parthenogenesis, except on the assumption that the parasites are held in position by a globular wall (*vide* Plate LXIV, Figs 44-47 of Thomson and Woodcock, 1922). Tobbs

P. ovale (Sinton, 1955)

Even as late as 1953, the Drafting Committee on "Malarial Terminology" appointed by the World Health Organization (Covell, Russell and Swellengrebel, 1953) are not agreed in an authoritative pronouncement on the matter. They state that "in this report the word 'in' has been used, but the possibility that the above (extracellular) theory is correct has not been overlooked."

From the evidence available it is seen that the relation of the plasmodium to its host cell at various stages of its development, still remains doubtful. A more exact knowledge of the physical structure of normal and parasitized erythrocytes would help to explain the various observations mentioned above. A renewed study of the migration of *P. vivax* should be made under fresh conditions in a moist chamber on a warm stage or in a hot room.

HAVE WE A PROPER PICTURE OF THE CYTOLOGICAL STRUCTURE OF THE MALARIA PARASITE?

The earliest work on the structure of the malaria parasite was carried out in fresh preparations. Since the advent of the Romanowsky stains half a century ago, few other methods of examination of malarial blood have been used.

These stains produce a beautiful picture of the plasmodia. They form the most reliable method of diagnosis. Unfortunately, this method of dry fixation and staining gives very varied results. It is not, therefore, recognized by most protozoologists as producing a reliable picture of the minuter and more complicated features of the cytological structure of most protozoa*. So much use has been made of this method of staining that the more reliable cytological method of wet fixation and iron hæmatoxylin coloration (Sinton and Mulligan, 1930) has been neglected. We have none of the very careful descriptions of the plasmodia as have been given by Wenyon and by Dobell in the study of the intestinal amœbæ.

*As Dobell once said— "The day is now past when one can go into the field with a bottle of Giemsa and hope to rival Schaudinn." This was also emphasized by an Editorial in the *Lancet* (1926).

Until this is done there will still remain many of the doubtful questions such as those detailed below. It is suggested that, on account of its slow growth and the presence of all stages of its schizogonic cycle in the peripheral blood, *P. mui* would form a most suitable subject for a study of this nature.

WHAT IS THE NATURE OF THE VACUOLE SEEN IN THE RING FORMS OF THE MALARIA PARASITES?

Grassi and Feletti (1890) describe the vacuole as a large clear bladder-like nucleus with a delicate, often invisible, nuclear membrane and a nucleolus (the chromatin).

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that the vacuole was formed inside the ring of protoplasm to give the young parasites

"The nature (i.e., whether nuclear or nutritive) of the 'vacuole' seen in the ring forms is still uncertain, so that provisionally the best term appears to be vacuole" (Covell, Russell and Swellengrebel, 1953) *

Not all modern malariologists appear to be in doubt as to the nature of the vacuole. For example, Le Dantec (1924) and many other workers describe the nucleus as vesicular with a karyosome, Boyd (1935) speaks of the nucleus of *P. vivax* as round or oval with a limiting membrane, within which is a karyosome formed of one or an agglomeration of many chromatin granules, and Thomson (1932) stated that the nuclear structure of a *falciparum* gametocyte is a definite vesicular one.

While there is little doubt that the 'vacuole' with its chromatin mass is a definite vesicular nucleus, further work with more precise cytological methods is needed to confirm this. A few trials made on *P. vivax* with the iron hæmatoxylin method of Sinton and Mulligan (1930), gave results which made the vacuole resemble very closely the limax type of vesicular nucleus seen with some intestinal amœbæ.

The absence of a vacuole is usually given as one of the diagnostic characters of the early stages of gametocyte growth. A careful study of these forms shows that the vacuole is still there but that the chromatin is evenly scattered through it, so obscuring its usual empty bladder like appearance.

The chromatin has a very close connection with the vacuole. In *P. mui* with its slow rate of growth this is very well seen at all stages (*vide* Sinton, 1934, Plates III and IV).

*Ewing in 1898 and later Rowley Lawson considered the vacuole as a small portion of the erythrocyte surrounded by two pseudopodia coalescing at their ends.

WHAT ARE THE CYTOLOGICAL CHANGES WHICH OCCUR WHEN THE MALARIA PARASITE SEGMENTS?

Few workers appear to have studied the details of the schizogony of plasmodia using well recognized cytological methods. Schaudinn (1902) described a sort of primitive mitosis in the asexual forms of *P. vivax*. In the same parasite, Ivanic (1937) described a form of promitosis going on to true mitosis in the later stages of schizogonous division. More recently Wolcott (1954) has studied the nuclear structure and division of *P. vivax*. He says that he never found the vesicular nucleus and karyosome reported by Ivanic (1937). However, he describes a mitotic stage in the cycle of schizogony with two chromosomes and a well marked achromatic spindle. He used wet films stained with Giemsa, so his observations require confirmation by more precise cytological methods.

Here again the slow rate of growth of *P. mui* and the abundance of all stages in the peripheral blood, should make this species an admirable one for the study of nuclear division. The early stages of chromatin division and their relation to the vacuole are shown in Plate VI, Fig. 25-28. At this stage of schizogony the findings suggest simple binary fission of a vesicular nucleus.

IS MULTIPLE INFESTATION OF ERYTHROCYTES IN MALIGNANT TERTIAN INFECTIONS DUE TO PREMATURE DIVISION OF YOUNG SCHIZONTS?

In very severe infection of *falciparum* malaria, it is not uncommon to find some red cells infested with many parasites, even as many as six per cell (Plate VI, Fig. 24).

Some workers suggest that this is due to binary fission of the young schizonts and not to the attack of the cell by several merozoites (Alessandrini, 1933).

Schuffner and de Graaf (1937) have discussed this hypothesis and come to the conclusion that this multiplicity of infestation was due to the greater attraction afforded by certain erythrocytes to the young parasites. Hingst (1934, 1938), however, attributes such multiple infections as due to amitotic division of young schizonts already infesting the cell rather than to multiple invasion of single merozoites.

DOES THE METHOD OF PREPARATION CHANGE THE MORPHOLOGICAL CHARACTERS OF THE PARASITE?

Sinton (1955) has discussed the causation of 'banded' forms in infections with *P. malariae* and *P. mui*. He has produced reasons to support the view that these are not found *in vivo*, but are distortions produced by the method of preparation of the thin film. They give indications of the physical condition of the parasite at the time that the film was made. They are valuable aids in diagnosis. Similarly with *P. tenue* the characteristic forms seen appear to be produced in a similar manner (Callanan, 1926). They indicate a special physical state of the plasmodium at the time. This shows a tertian periodicity.

WHAT IS THE NATURE OF THE CHANGES IN THE ERYTHROCYTES INFESTED BY MALARIA PARASITES?

WHAT CAUSES THE CHANGES IN THE SIZE AND SHAPE OF INFESTED ERYTHROCYTES?

The enlargement of the infested red cell in *vivax* infections is well known. On the other hand, the æstivo autumnal parasite in its later stages is found more commonly with a smaller cell, which may show marked colour changes when examined in the fresh. We have still to discover the different causations of these changes.

The oval and fimbriated erythrocytes, which are seen in thin films of the h *P. ovale* and *P. knowlesi*, are often of .) has discussed the probable causation in *vivax* but are produced mechanically during the preparation of thin films which dry very quickly, they indicate a special physical character of the cells.

WHAT IS THE CAUSE OF THE DIFFERENT TYPES OF "STIPPLING" SEEN IN ERYTHROCYTES INFESTED BY DIFFERENT SPECIES OF PLASMODIUM?

Schuffner (1899) was the first to describe these changes. He considered that the Schuffner's dots of *vivax* infections were due to degenerate particles in the stroma of the infested red cells.

These changes were examined in some detail by Maurer (1901, 1902), who gave the same reason as Schuffner for the stippling seen in *vivax* infections. In the case of the "red-coloured dots, little rings and lines" with the *Laverania* species (Maurer's dots), he concludes that these were due to "changes or losses of substance on the upper surface of the erythrocytes, which are the result of the attacks made by the parasite in order to adhere to its host cell and to obtain nourishment." The numbers are said to increase with the size of the parasite and are not stationary as with *vivax* stippling.

Billet (1909) seems to have had the same description of the dots. He agrees with Maurer's explanation of the dots as being due to mechanical changes in the thin films. He also describes the dots as being due to the pseudopodia to some of these spots, which he believes are either a secretion of the parasite or a little of its own substance. The number of the dots is thought to be a function of the amœboid activity of the parasite species.

The exact nature of these markings is still in doubt. In addition to the dots described by Schuffner, there are other bodies described by various writers. These include the "dark red" bodies and the "dark red" bodies and the "dark red" bodies. A dark red deposit around segmenting forms is reported and discussed by Sinton and Mulligan (1933b), Sinton (1934), and Mulligan (1935) in all three species of oriental simian plasmodia. Malamos (1934) found a capsule with *P. vivax*, *P. ovale* and *P. knowlesi*. Garnham (1931) and Thomson (1933) investigated curious bodies seen in red cells with immature gametocytes of *P. falciparum*.

Stuppling and similar changes have been seen in infections with most kinds of malaria infection * The demonstration of these markings depends very largely upon the type and intensity of the stain used The use of alkaline distilled water,

In the same category of changes comes the "capsule" which is sometimes so conspicuous around deeply stained crescents This is discussed by Garnham (1931, 1933) and Thomson and Robertson (1932) Warasi (1932) thinks that the parasite is covered by two membranes, first the periplast of the red cell and second the periplast of the parasite Between these two is the hæmoglobin, and as the parasite grows, this disappears and the two membranes fuse together to form a capsule Apart from this, Mannaberg (1894) states that in fresh preparations a perfectly recognisable double capsule is seen

Many of the appearances seen support the idea of Schuffner (1899) that the origin of Schuffner's dots is different from Maurer's ones The latter look as if they were produced directly by the parasite and were not merely due to degenerative changes in the erythrocyte

ARE MORE THAN ONE SPECIES OF PARASITE INCLUDED UNDER THE NAME OF "*PLASMODIUM FALCIPARUM*"?

Even from the earliest days of the separation of the crescent-forming parasites from the quartan and tertian ones, there has been doubt as to how many species of parasite were included in the former category These were first divided by the supposed periodicity of their febrile paroxysms Later morphological differences were described as well as variations in their febrile reactions, in the effects of treatment, and in their susceptibilities to infecting the same insect host

WHAT IS THE DURATION OF THE ERYTHROCYTIC CYCLE OF SCHIZOGONY OF THE ÆSTIVO AUTUMNAL MALARIA PARASITES?

The earlier workers on the malaria parasites, such as Marchiasava, Bignami and Grassi considered that there were two kinds of æstivo autumnal parasites—a tertian one and a quotidian Mannaberg (1894) divided them into a tertian and two quotidians Even as late as 1914, Manson following the last worker grouped them as (a) Subtertian due to *Laverania malarie* (syn *P falciparum*), (b) Pigmented quotidian due to *P præcox*, and (c) unpigmented quotidian due to *L immaculata*

The fever curve in these infections is very often remittent, not intermittent, so that they may appear to have a quotidian periodicity In recent years all these forms have been grouped as "malignant tertian", and the absence of tertian febrile periodicity explained as due to the schizogony of all the parasites not being simultaneous but distributed over several hours Why such an abnormal schizogony

*The dots seen in quartan malaria are often called Ziemann's but Seyfarth (1924) mentions them as Brug 1

should occur in this species of malaria parasite and not in the other three infecting man, seems curious, unless this is another difference possessed by the genus *Laverania* as compared with the genus *Plasmodium*.

Even although the term 'malignant tertian' is now used by most English writers, there still seems to be great doubt as to the duration of the cycle of erythrocytic schizogony. Various authors give this as 24-28 hours, 36-40 hours
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The prolongation of the febrile paroxysm in these supposedly tertian infections could be accounted for by a double infection, such as gives rise to quotidian periodicity in some *unax* infections. It is possible, however, that the older workers were correct, and that a true quotidian species occurs as in the case of *P. knowlesi* in simian malaria. Indeed, Craig (1909, 1921) has reported such a parasite, which he named *P. falsiparum quotidianum*. Row (1917) also describes and pictures the parasites seen in a culture of 'quotidian malaria' (*Laverania praecox*).

One needs more careful study along the lines used by Sinton (1934) and Mulligan (1935) to determine the duration of the cycles in the species of monkey malaria. Sinton (1922) using this method showed that *P. tenue* had a definite tertian periodicity. Cultural methods might also be useful. The strains used would be more easily studied under conditions of malaria therapy. It is suggested that possibly strains from the North-West of India should be compared with those from the Eastern parts, and African ones with Italian.

From this it is seen that the question still remains unsolved as to whether all 'malignant tertian' parasites have a true tertian periodicity, i.e., are only one species.

CAN SEVERAL SPECIES OF ÆSTIVO-AUTUMNAL MALARIA PARASITES BE SEPARATED BY THEIR MORPHOLOGICAL CHARACTERS?

While the older writers separated their different species of the *Laverania*

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The sinking of all these crescent forming plasmodia in one species—*P. falsiparum* (*P. praecox*, *P. immaculatum*)—seemed to settle the question, but in more recent years many workers have doubted the unity of this species. For example, Ross (1911) was still inclined to believe that there are two or three species in this group. O Gorman-Lalor (1913) reported the unusual morphology of such parasites in a blackwater-fever area in India. Marchoux (1922) points out differences between African, Italian and Macedonian forms. Schuffner and Hylkema (1922) reported what they thought was a special form during an epidemic at Belwan in Sumatra, many other workers are also doubtful.

The American worker, Craig (1909, 1921) describes what he considers to be a new variety of *P. falciparum* which he has named *P. falciparum quotidianum*

Grave doubt has been cast by many workers on the unicity of the Italian and the African forms of *P. falciparum*. Ziemann (1915) thought that the form found in the Cameroons, West Africa, was so different from the Italian form that he named it *P. perniciosum*, and has since described it in comparison with other forms of *P. falciparum* (Ziemann, 1938)

James and Kauntze (1930) considered that the malignant tertian parasite seen by them in East Africa differed from the classical description of *P. falciparum*. Many Italian workers noted differences between the Italian parasite and some found in Abyssinia. The latter parasite has been named by Giovannola (1938) as *P. falciparum ethiopicum*

A curious type of *P. falciparum* was found by Marzinowsky (1916) in South Russia, which showed segmenting forms in the peripheral blood. This he named *P. caucasicum* *

The species most in dispute has been *P. tenue*, described by Stephens (1914) from specimens received from the old Central Provinces in India, and later from West Africa (Stephens, 1915)

Sinton (1922) carefully examined five cases from Nagpur Jail, and was convinced that this was a separate species of malignant tertian parasite. Since then other data have been collected to support this conclusion.

In the Indian sub continent there seem to be at least two morphological species of *Laverania*—(i) the ordinary classical form, only seen with small rings in the peripheral blood (except in pernicious cases), occurring commonly in the north western parts of the country, and (ii) the large-ringed form (small rings may sometimes be detected in the very early stages) common in the eastern and southern parts of the country. It is the latter parasite which shows a "tenue" stage †. Every year blood films taken from cases in the latter parts of India, were given to the post graduate students in our Annual Malaria Class. Students from the northwestern areas almost invariably diagnosed these initially as *P. vivax*,

extreme rarity there, while they are relatively common in those from some of the eastern parts of this sub continent (Sinton, 1927)

Apart from the 'tenue' stage with its tertian periodicity, the parasite is seen for a longer time in the peripheral blood, even as late as 36th hour of its cycle, and the rings are much larger than the classical *P. falciparum*. The pigment sometimes

* In the winter of 1934-35 some slides were sent me from Gilgit in Kashmir showing parasites resembling those described by Marzinowsky (1916). Unfortunately the specimens were mislaid before a full investigation could be made.

— morphological characteristic of this parasite the method of preparation of the parasite at one stage seen found in the cycle an earlier point in its

seen in the largest rings is finer, more scattered and lighter in colour than the coarser dark brown or jet-black masses seen in *P. falciparum* at a similar stage. The golden yellow colour of this pigment was well seen in the only mature schizont (Plate VI, Fig. 23) observed in Sinton's cases, and which contained eight merozoites (*cf.* Marchoux, 1926). The Maurer's dots seen in the classical *P. falciparum* are usually described as irregular in shape and few in number, and as often being difficult to demonstrate. In *P. tenue* they stain more easily, and are more numerous, rounded, linear and coccoid in shape (Plate VI, Fig. 22).

These forms have been reported by workers in many other tropical countries, for example Hucks and Bowden (1924) and Darling (1925) in the United States, Perekrupoff (1917) in Russia, Sergeant *et al.* (1913) and Vialatte (1922) in North Africa, and Jerace (1932) in Italy, among a host of others. I have received beautiful slides of this form sent by Dr G. Fraser from Assam and Dr K. L. Rustomjee from Ceylon. Russell (1928) gives a careful review of the literature up to that date.

Is the small ring form that of *crassa* or *tenue* or *immaculatum* or *precocum*?

and Mulligan (1933*a*, 1933*b*) were unable in the cases of *P. knoulessi* and *P. cynomolgi* to find that such conditions caused any morphological changes in the character of these parasites.

In spite of the evidence produced, the latest authoritative statement says—" *P. tenue* Stephens, 1914, is no longer accepted as a distinct species " (Covell *et al.*, 1953).

If *P. tenue* be accepted as a true species, what is its proper specific name? The parasite is probably the same as one of those originally described as either *P. precocum* or *P. immaculatum*. As pointed out by Christophers and Sinton (1938) both these names are invalid as having first been used to designate avian parasites. Similarly, the specific name *tenue* is also invalid, because a few months before Stephens (1914) used it, a parasite of the Peking nightingale had been named *Hemamoeba tenuis* by Laveran and Marullax (1914). Ziemann (1915), in his discussion of the human parasites, names it in his description of the figures given on his plate—" *Plasmodium khartunense* (From Khartoum). Synonym *Plasmodium tenue* Stephens "

ARE THERE CLINICALLY DIFFERENT STRAINS OF THE ÆSTIVO-AUTUMNAL PARASITE?

Apart from the question of the periodicity of the febrile paroxysms, other distinct clinical differences have been reported between 'malignant tertian' infections in various parts of the world.

When James (1932) compared the Rome strain of *P. falciparum* with an Indian one, he found that it needed almost ten times the dosage of quinine to control the former infection, which was, however, easily affected by atebrian. In the Panama, very heavy doses of quinine, as compared with European practice, are required to reduce pyrexia. Fairley (1946) has reported that almost double

the normal dosage of atabrin was necessary to suppress some *falciparum* infections in the Aitepe-Wewak area of New Guinea. Other workers in describing their new species have noted clinical differences.

O'Gorman Lalor (1913) and Hassal-Wright (1920) drew attention to unusual forms of the parasite found in blackwater-fever areas of India. Sinton (1927) remarked upon the similarity of the recorded distribution of *P. tenue* and the same syndrome. Cort (1929) noted a special form of subtertian parasite in association with hæmoglobinuria, a relationship between *P. falciparum* and hæmoglobinuria in drawing attention to the text book descriptions, conclude that "the subject certainly merits careful enquiry in Kenya and Uganda, particularly in districts where blackwater fever occurs."

FAILURE TO INFECT SOME ANOPHELINES WITH FOREIGN STRAINS OF *P. FALCIPARUM*

James, Nicol and Shute (1932) found great difficulty in getting any infections in *A. maculipennis* var. *atroparvus* with Indian strains of *P. falciparum* as compared with the Rome one, although clinically the latter was more pathogenic to man. This was confirmed by Shute (1940) with other strains of tropical origin.

Raffaele and Lega (1937) remark upon the difficulty of infecting *A. maculipennis* with their new variety, *P. falciparum aethiopicum*. Similar results with both *P. falciparum* and *P. vivax* have been recorded in America.

As we do not know what are the factors which govern the susceptibility of mosquitoes to any malarial infection, it is not possible to decide whether these failures are due to something in the insect or something in the parasite, either of a strain or a specific character.

WHAT IS THE FATE OF THE SPOROZOITES IN THE INSECT HOST?

Ross (1905) in describing his original discovery said—"I saw the thread like bodies, although apparently without motion themselves, were soon scattered by the insect's circulation all through its body". This passive distribution was also noted by Grassi and Schaudinn. Muhlen (1921, 1931) showed that the sporozoites could be found in the muscles and even in the legs and in the appendages of the head.

The concentration of these forms in the salivary glands is great, but it is uncertain whether this is due to chemotaxis or purely a matter of chance (Schaudinn, 1902). It is easy to understand how the sporozoites in the salivary glands are got rid of in the acts of biting, but the fate of the others is still uncertain.

In the early stages of the infection, at least, if a piece of a segment of a leg is severed from an infective living insect and the fluid expressed from it, this is found to contain large numbers of sporozoites. What is the ultimate fate of these? Are they infective? Do they form a reservoir from which the supply in the glands is replenished as these become depleted by biting? How long can they be detected and are the insects still infective after they disappear from the appendages?

Schuffner, Korteweg and Swellengrebel (1929) found that in the autumn the bites of one or two mosquitoes failed to cause malaria in the usual incubation period, but infection appeared after eight to nine months. The impression formed by me while working in the Malaria Laboratory at Horton was that, with the Roumanian strain of *P. vivax*, these prolonged incubations occurred more often when the sporozoites had been present for several weeks in the insect host. Were these latent infections caused by sporozoites which had been a long time in other parts of the insect's body? Did this give rise to senility of these parasites or was it merely a smaller dose of infection that was injected?

WHY ARE SOME SPECIES OF ANOPHELINES SUSCEPTIBLE TO HUMAN MALARIAL INFECTIONS WHILE OTHERS ARE NOT?

It is well known that the gametocytes of all the human species of *Plasmodium* will become gametes and conjugate to form zygotes, when taken into the stomach of even culicine mosquitoes. These zygotes never develop further in culicines and only in certain species of anophelines. As mentioned above the zygotes of some strains of parasite may behave in a refractory manner in anophelines which are normally susceptible to such infection of other strains.

Why this occurs has never been determined. Is it due to some factor in the insect or some in the parasite? The best researches on the subject have been those of Huff (1934), but even these have failed to give a satisfactory explanation.

MISCELLANEOUS QUESTIONS

- (i) WHAT IS THE MALARIA 'TOXIN' AND WHAT IS THE CAUSE OF THE MALARIA PAROXYSM?

Is there no true malaria toxin? Is the paroxysm due to a condition of anaphylactoid shock caused by the discharge into the blood stream of particles of pigment, remains of parasitized blood cells, and pieces of parasite at the moment of schizogony (Sinton *et al*, 1928)?

- (ii) CAN DIFFERENT IMMUNOLOGICAL STRAINS OF PARASITE BE DIFFERENTIATED BY DERMAL OR BY SEROLOGICAL TESTS?

Sinton and Mulligan (1932) showed that an antigen prepared from an almost pure suspension of *P. knowlesi* produced a marked dermal reaction with animals infected with a similar parasite. Could this method be used to differentiate the different strains of this parasite?

Before it became possible to isolate large quantities of parasite substance (Sinton and Mulligan, 1932), many experiments were made to perfect a complement fixation test. Could a better antigen now be produced which would give a differential diagnosis, between the species or even the strains of monkey malaria?

Several precipitin tests have been tried for malarial infection. The results in these appear to depend merely upon their effects upon the increased globulin content of the blood, and as such are poor diagnostically.

(iii) WHAT IS THE NATURE OF THE ANTIBODIES IN MALARIA?

From a study of malarial immunity it is evident that two factors are involved—an anti parasitic one and an anti toxic one (Sinton 1939). The former acts by a destruction of the parasites and the latter by neutralizing their effects.

Is the anti parasitic one a lysin which renders the parasites more readily destroyed by the macrophages or is it an opsonin which causes the macrophages to attack the parasites with greater avidity?

While we have no information as to the nature of the anti toxic one, we can only consider its results.

Does it pass through the placenta and so cause a passive immunity in the foetus or does the latter produce its own antibodies under the stimulation of malarial 'toxin' entering its circulation from the blood of its mother (Sinton 1939a)? Can acquired maternal immunity be transmitted through her milk?

(iv) WHAT IS THE ORIGIN OF THE GAMETOCYTES?

Are these derived from special exoerythrocytic merozoites or from the blood ones? Probably at least from the latter, as they occur after blood inoculations.

At what stage of their development do these forms take on their sexual character, or are they so *ab initio*? Do they have an intracellular position as compared with asexual forms, and if so would this determine their fate? Does the environment in which they develop have any effect upon their fate, i.e., do the special conditions of the spleen and bone marrow have any action in determining their development into sexual forms?

(v) WHAT SPECIES OF PLASMODIUM OCCUR IN THE LOWER MONKEYS OF AFRICA?

Sinton and Mulligan (1932a, 1933), Mulligan (1935) and Sinton (1934) made a careful study of the malaria parasites of the lower monkeys of the Old World.

Those from Asian countries were found to be infected with at least three distinct species—(a) *P. knowlesi* Sinton and Mulligan, 1932, having a 24 hour cycle of schizogony in the erythrocytes (b) *P. cynomolgi* Mayer, 1907, with a 48 hour cycle, and (c) *P. inui* Halberstadter and Prowazek, 1907, with a 72 hour cycle. Among the lower African monkeys, *P. gonderi* Sinton and Mulligan, 1932 (vel *P. kochi* Gonder and Berenberg Gossler, 1908) and *P. kochi* Laveran, 1899, with varieties were described. The latter parasite has since been found not to be a *Plasmodium* but to belong to the genus *Hepatocystis*.

Except for the careful studies made by Gonder and Berenberg Gossler (1908), Berenberg Gossler (1909) and Gonder and Rodenwaldt (1910), the plasmodial parasites of the lower African monkeys seem to have had little attention. Is *P. gonderi* identical with *P. cynomolgi*? How many African species are there?

SUMMARY

It is pointed out that there are many unsolved problems in our knowledge of malaria parasites and these are discussed

- 1 Should genus *Laverania* be again separated from the genus *Plasmodium*?
- 2 Is the malaria parasite inside or outside the host erythrocyte?
- 3 Have we a proper picture of the cytological structure of the malaria parasite?
 - (a) What is the nature of the 'vacuole'?
 - (b) What cytological changes occur when the parasite segments?
 - (c) Are multiple infections of the red cells due to simple binary fission and not to invasion by multiple parasites?
 - (d) Is the morphological appearance of the parasite in thin films influenced by the method of preparation?
- 4 What is the nature of the changes in parasitized erythrocytes?
- 5 Does the present species '*P. falciparum*' contain more than one species?
 - (a) What is the duration of the cycle of schizogony?
 - (b) Can several species be separated by their morphology?
 - (c) Do the infections caused by these species vary clinically?
 - (d) Do they vary in their ability to infect anophelines?
- 6 What is the fate of the sporozoites in the insect host?
- 7 Why are some species of anophelines susceptible to malarial infection while others are not?
- 8 Miscellaneous questions
 - (a) Is there a malaria 'toxin'?
 - (b) Can different immunological strains be separated by laboratory tests?
 - (c) What is the nature of the 'antibodies' in malaria?
 - (d) What is the origin of the gametocytes?
 - (e) What species of *Plasmodium* occur in the lower monkeys of Africa?

REFERENCES

- ALEMANDRINI G (1933) *Arch f Protist* 79, p 336
 ARGUTINSKI P (1903)
 BERENBERG-GOSSLER H VON (1909)
 BIGGER A (1913)
 BLACK R H (1948)
- BLANCHARD R and LANGERON M (1913)
Kenya E Afr Med J, Oct, 3, p 18.
Bull Soc Path Exot, 10, p 841
Brit Med J II, p 1130
- How to do a Malaria Survey* 3rd Ed Manager of Publications Delhi

SOME EVOLUTIONARY POSSIBILITIES IN THE HISTORY OF THE MALARIA PARASITES

BY

REGINALD D. MANWELL

(*Department of Zoology, Syracuse University, Syracuse, New York*)

[July 28 1955]

THE problem of the evolution of the malaria parasites is, in the nature of things, one which can never be wholly solved but its very difficulty makes it the more challenging to the medical men and to the biologist. It is a question which has puzzled malarialogists almost ever since the causative organisms of malaria were discovered, some 75 years ago, and perhaps we are even now not much nearer a solution. Yet so much new light has been shed on what may be called the natural history of malaria in the past decade or two, that it is worthwhile taking a new look at the problem.

Involved, of course, are not only the parasites themselves, but their hosts, both vertebrate and invertebrate. When biological relationships are of kinship of existing species of tell us little of what we might call the third dimension of the problem, or time. And the ancestral relationships are those in which are we most interested. From what did the malaria parasites evolve? What may have been their earlier hosts? What light, if any, can be thrown on the evolutionary development of the complex life cycle of this genus of parasites?

The best evidence for the evolutionary history of any living thing is undoubtedly that afforded by fossils, but fossil malaria parasites are, of course, non-existent, as indeed are fossil remains of most other parasitic organisms. Yet fossil Foraminifera are known from Cambrian times (some 500 million years ago), and Radiolaria may be even older, having been reported from rocks of pre-Cambrian age (Chapman, 1902, Pirsson and Schuchert, 1924, Glaessner, 1945). Both groups of Protozoa are free living, and both are almost exclusively marine, and their antiquity is therefore, only of interest here because it shows the great age of the phylum, but it suggests that the parasitic protozoa may also have had a very long evolutionary history.

Indeed, it may safely be assumed that there were protozoa of at least the two orders just mentioned long before the oldest of these fossils were laid down, for the morphology of many of the latter is much like that of contemporary forms, and it is, therefore, probable that their life-histories were also similar. Since the life-cycles of the relatively few of these organisms which have been thoroughly studied are complex, including the production of gametes and fertilization evolution must have already gone a very long way even in pre-Cambrian times. It seems likely that life-cycles as complex as those exhibited by such parasites as the malaria plasmodia were even then commonplace.

Additional evidence that this was probably the case is furnished by the occurrence of fossil algae in rocks of the same age. Algae are closely related to the plant malar life cycles, also. They are also known to have been present perhaps 140,000,000 years ago. *Calophora* and *Sporozoa* are unknown in the fossil state, although since some of the former have skeletons or tests it is not impossible that such remains may eventually be found.

Of course, one must suppose that free living organisms antedated those of parasitic habit, and living ancestors. Sandon (1932) refers to some unicellular organisms, previously accustomed to nourishing themselves after the manner of plants, began to eat the bodies (either living or dead) of their neighbours. "Some parasitic protozoa are perhaps, even now, not far removed from that stage, since they closely resemble free-living species. But the Sporozoa, all of which are parasites, resemble no free living protozoa known to day, and as the great protozoologist, Gary N. Calkins, used to say in his lectures many years ago, they represent a group the members of which are so different that it is often impossible even to suppose any mutual relationship. Thus, however ancient some of the free-living protozoa may be, we have no direct evidence bearing on the evolution of the parasites of plants and animals."

The malaria parasites are classified as *Hemosporidia*, subclass of the *Telosporidia*. This subclass contains two families which are certainly very closely related, the *Hæmoproteidæ* and the *Plasmodiæ*, to the second of which belong the malaria parasites. Both families are large as far as the number of species is concerned, but small in the number of genera contained. There are at least 50 recognized species of *Plasmodium*, the only genus of the *Plasmodiæ*, and probably many more species of *Leucocytozoon* and *Haemoproteus* (the two genera comprising the *Hæmoproteidæ*).

The second order in the class *Hemosporidia* contains only the single family *Babesidæ*, together with two genera of doubtful status *Dactylosoma* and *Toxoplasma*.*

* According to the classification of Hall (1933)

The Babesias are parasites of red cells, and superficially resemble the malaria plasmodia, but although they are incompletely known, the two orders do not appear to be closely related. Both vectors and life-cycles differ considerably.

It has long been thought that the malaria parasites may have originated from the coccidia. Mesnil (1899) seems to have been the first to point this out, and the view was supported by Schaudinn (1899), and later by Reichenow (1912). Wenyon (1926) spoke of the affinities existing between coccidia and the hæmosporidia, from the first of which the second group "may be supposed to have evolved."

The evidence for the belief that the malaria plasmodia (and presumably also their close relatives, the genera *Hæmoproteus* and *Leucocytosoon*) arose from the coccidia, lies in the close similarity of their life cycles. All of these organisms are typically cell parasites, and all exhibit sexual stages. The coccidia are generally parasites of the intestinal epithelium, in the cells of which they undergo a number of asexual generations, culminating in the production of gametes. After fertilization, the zygote develops into a resistant oocyst, containing sporocysts which in turn contain sporozoites. These constitute the infective stages, and initiate a new infection after ingestion by a fresh host. There is no vector (but sometimes an alternation of hosts), and hence resistant stages are generally necessary for survival without the host.

The life cycles of the malaria parasites are obviously very similar to this pattern, the chief differences being the addition of a second host which, in all species where the life-histories have been completely studied, is a mosquito, and the lack of a resistant oocyst stage. The fact that the parasites reside in the erythrocytes of the vertebrate host, rather than in the intestinal epithelium, seems of much less significance than it did before the exoerythrocytic stages of the cycle were discovered two decades ago.

The chief controversy revolves around the question of whether the ancestral organisms from which the Plasmodiæ evolved were parasites of invertebrates, and therefore presumably of biting flies (such as mosquitoes, hippoboscids, *Simulium*, and others), or of the vertebrates. And if it is conceded that this family may first have been parasites of vertebrates, were their hosts in the beginning perhaps reptiles, since it was from the latter class that both birds and mammals evolved?

These problems are all left as yet to be solved.

do not occur in insect hosts

The fact that most coccidia are parasites of the gut suggests that they were originally acquired as the result of ingesting food or water contaminated with them. Of course, the forms from which they evolved must once have been free-living, although it is at least conceivable that they may have parasitized invertebrates before becoming adapted to life in vertebrate hosts, and that the latter were first infected by ingesting the former. In any case, it seems probable that these ancestors of the coccidia of vertebrates had already developed a highly complex life-cycle,

just as those protozoa we know as fossils must have done. Doubtless cysts, the production of which often climaxes a period of asexual reproduction and may also involve a sexual cycle, were the infective stage. Certainly a good deal of adaptation must have been required for life within a living host, but protozoan cysts have often been observed to survive passage through the intestine and some free-living species may even persist there for a limited time.

Huff (1938, 1945) has urged the point of view that the malaria plasmodia and their close relatives were at first parasites of insects, and became secondarily adapted to life in vertebrates after their insect hosts developed the blood sucking habit. The fact that these parasites do not seem to be pathogenic to their vectors favours this theory, and yet, as Ball (1943) has rather convincingly maintained there are too many exceptions to the rule that the degree of pathogenicity is inversely related to the duration of association between host and parasite to make this type of evidence more than doubtfully suggestive.

Huff also emphasizes the fact that the life cycles of the *Hæmoproteidæ* and *Plasmodiæ* are more similar as far as the insect host is concerned than for the vertebrate host. This is true (although we still know little or nothing of the life histories of many species), but it is worth pointing out that the newer knowledge of the vertebrate portions of these life cycles makes them seem ever more alike.

The known insect hosts of the *Hæmoproteidæ* and *Plasmodiæ* include hippoboscids flies (*Hæmoproteus*), *Simulium* (*Leucocytozoon*), and mosquitoes (*Plasmodium*). The first of these vector groups is only distantly related to the last two, and it may (as Huff concedes) suggest—despite the undoubted similarity of the insect portions of the life cycles of all three genera of blood parasites—that this portion of the cycle developed later than that in the vertebrate host.

But, in any case, the insect-vertebrate type of life cycle characteristic of *Plasmodium* evolved before the ancestors of the present day vertebrates. That this dietary requirement may have been the fact that it is, even today, restricted to females. As for the antiquity of mosquitoes, sufficiently like those of today to be recognizable as such, they are known from Eocene times, some 60 million years ago. A fossil form, believed to be a male mosquito (note the plume-like antennæ), found by the writer in the famous Oligocene shales of Florissant, Colorado is shown in Plate VII, Fig. 1. Mosquitoes are, of course, older than this, and doubtless this is also true of other blood sucking Diptera. Diptera as a group appeared as early as the middle Jurassic, but they were at first restricted to midges and crane-fly like forms (Carpenter, 1953). The oldest known fossil insects (notably the extinct Palæodictyoptera and cockroaches) were extant in the later Carboniferous period, which is believed to have been about 250 million years ago. It is worth noting that insect evolution had gone a long way even then, and it is very likely that insects were already well supplied with protozoan and other parasites.

The classes of vertebrates to which the known natural hosts of the malaria plasmodia belong include, as perhaps we should expect, all those of terrestrial habitat. But susceptible host species are not evenly distributed among these classes,

*Malaria parasites have also been reported from the bull frog by Fantham, Porter and Richardson (1942) but nothing else is known about them.



3

FIG. 1. A fossil mosquito (male) from the famous Oligocene shales of Florissant, Colorado. (Note the

nor are such species relatively numerous. Most of the known reptilian host species of plasmodia are lizards, and the majority of avian hosts are passerines. There is much more variety among the malaria-susceptible species of mammals.

The striking parallelism between the reptilian and avian species of *Plasmodium* has often been noted. Together these species constitute almost two-thirds of the recognized species of the genus. Unfortunately very little is yet known about the life cycles of the malaria parasites of reptiles, but the resemblances in morphology of the avian and reptilian types point to a close relationship. It may be that such similarities are to be explained as due to parallel evolution, but it seems more likely to be the result of relatively slow evolutionary change on the part of the parasites since the original separation of avian and reptilian stocks, even though bird and lizard lines of descent must have diverged at a very early period.

The relatively small number of malaria susceptible species among the mammals, and their spotty taxonomic distribution (antelopes, water buffalo, rodents, primates, bats, to mention the more important) seems to suggest that malaria among them was a kind of after-thought on the part of nature. Perhaps the greater pathogenicity of some of the mammalian species of *Plasmodium* points to the same conclusion.

Another fact which may support the belief that malaria was originally a disease of reptiles, and then also of birds, is the very common occurrence of the two closely related genera* of blood protozoa, *Hemoproteus* and *Leucocytozoon*, among birds and, in the case of the former, among reptiles also. As with the avian malaria, infections of *Hemoproteus* and *Leucocytozoon* seem usually to affect the host very little, a fact which seems to indicate a very long period of host-parasite association.

Still another fact which is in accord with the possible earlier occurrence of malaria in reptiles and birds is the fact that the vectors of malaria are notremes, reas birds (Romer, Diptera, and, especially, the blood sucking types now serving as vectors of malarial and malaria related parasites. (But it must be remembered that the vectors of the great majority of species of *Plasmodium* are still unknown, and there is no certainty that all are mosquitoes. It is also true that the vectors of most species of *Hemoproteus* and *Leucocytozoon* still remain to be discovered.)

The occurrence among the coccidia of genera such as *Shellackia* and *Lankesterella* (family Lankesterellidae), in which a life-cycle not unlike that of the *Hemosporidia* occurs, has often been regarded as supporting the theory that parasites of this group originated in vertebrate rather than invertebrate hosts. Perhaps this is best regarded as simply the result of parallel evolution, but it certainly indicates that the original hosts of parasites such as these need not have been insects, for here the cycle involves in the one case (*Shellackia*) lizards and mites,

*There are also certain hematozoa of mammals which are put into the genera *Hemoproteus* and *Leucocytozoon*. These are the *Hemoproteus* of monkeys and certain malar parasites of bats. Perhaps be regarded as the mammalian analogs. Hunt, 1917, Garnham, 1945 54. Manuall, 1916,

and in the other frogs and leeches. The nature of the cells parasitized in the vertebrate hosts also certainly suggests that the coccidian ancestors of the *Haemosporida* may have developed along similar lines, for *Shellackia* multiplies in the intestinal epithelium of lizards, the sporozoites later entering erythrocytes, and *Lankesterella* reproduces in the endothelium of the capillaries of the frog, with subsequent sporozoite invasion of the red cells. The tissue stages may be regarded as corresponding to the reproductive stages of *Haemoproteus* and *Leucocytozoon* in the vertebrate, and to the exoerythrocytic forms in malaria.

In the light of the occurrence of life cycles such as these among certain of the coccidia, it is rather tempting to think of *Haemoproteus* as perhaps the oldest

(hippoboscids), presumably indicating a long period of evolution on their part, points to alike conclusion.

Leucocytozoon may have originated later, and still seems to be confined to

red cells
would

Little can be said as to the possible or probable mutual relationships of the different species of *Plasmodium*. The life cycles of all, as far as is known, are similar, and follow a pattern similar to that in the genus *Haemoproteus* and *Leucocytozoon*. It might be thought that those avian and reptilian species of *Plasmodium* which most closely resemble one another arose the one from the other. This may, of course, have been the case, but parallel evolution may also have occurred. It is possible to divide species of the genus according to whether the gametocytes are elongate, or round or irregular, and according to the nature of the tissue stages. In the avian group, the types are *Plasmodium gallinaceum* and *Plasmodium falciparum*. In the reptilian group, *Plasmodium* of reptiles exhibits both kinds of gametocytes (see Huff, 1944). On the whole, although such characteristics afford convenient bases for classification, so little is yet known about the cycles of most species of *Plasmodium* (and this is equally true of species of *Haemoproteus* and *Leucocytozoon*) that it does not now seem worthwhile to try to work out the detailed relationships of any of these parasites.

*Falls *et al.* (1931) and Cook (1954) have shown that *Leucocytozoon simondi* may invade erythrocytes; the writer has also observed this in other species occasionally.

ABSENCE OF CROSS-IMMUNITY BETWEEN *PLASMODIUM* *CYNOMOLGI* AND *PLASMODIUM GONDERI*.

BY

P C C GARNHAM

AND

R S BRAY

(London School of Hygiene and Tropical Medicine)

(July 21 1955)

THREE species of *max* like malaria parasites are known to occur in lower monkeys *Plasmodium cynomolgi* (Mayer, 1907) in oriental macaques (chiefly from Malaya), *P. gonderi* (Rodhain and van den Berghe, 1936) in African mangabeys (chiefly from Belgian Congo) and *P. simium* (Fonseca, 1951) in Brazilian spider monkeys. All three species are much alike: they exhibit a tertian periodicity in the blood, cause enlargement of the erythrocyte accompanied by Schuffner's stippling, and morphologically resemble *P. max* in the asexual and sexual stages. When Sinton and Mulligan (1933) tried to disentangle the muddled systematics of *max* parasites, they found that *P. gonderi* and *P. simium* were very similar, and they suggested that *P. gonderi* was a subspecies of *P. simium*. Rodhain and van den Berghe (1936) found that *P. gonderi* had a cycle in the blood occupied 48 hours and that it could, therefore, hardly be called a sub-

never been isolated, from the descriptions given by Fonseca (1951), this South American representative of simian benign tertian malaria parasite has no features distinguishing it from other members of the group.

Strains of malaria parasites behave differently in their immunity reactions. Avian species as a whole have a wide spectrum of immunity, the larger species

et al., 1955), so-called strains of *P. falcatiparum* and *P. vivax* are so different (immunologically and in other ways) that they sometimes receive sub-specific names. Rodham (1954) has recently used the absence of cross-immunity between *P. bergi* and *P. vivax* as confirmation that they represent distinct species.

We felt that it would be useful to discover if cross-immunity tests would give a clue to the specific status of *P. cynomolgi* and *P. gonderi*. We possessed a number of monkeys highly immune to the former, and thus had a good opportunity of carrying out the requisite experiments

IMMUNIZATION OF MONKEYS.

Four *Macaca mulatta* (Numbers 81, 99, 101, 102) were immunized against *P. cynomolgi** by blood and sporozoite infections as shown in Table I.

TABLE I

Immunization of monkeys against P. cynomolgi.

Monkey Number	Date of first infection with <i>P. cynomolgi</i>	Mode of first infection	Superinfection with <i>P. cynomolgi</i>		
			Date of super infection	Mode of super-infection	Subsequent course of infection
81	May 29, 1951	Sporozoites	14/5/53 24/8/53 28/7/54 2/2/55	Blood Blood Sporozoites Blood	* * * †
99	April 25 1952	Sporozoites	14/5/53 24/8/53 28/7/54 2/2/55 25/2/55	Blood Blood Sporozoites Blood Sporozoites	† † † † †
101	July 23, 1952	Blood	14/5/53 24/8/53 28/7/54 2/2/55	Blood Blood Sporozoites Blood	† † † †
102	July 23, 1952	Blood	14/5/53 24/8/53 28/7/54 2/2/55	Blood Blood Sporozoites Blood	† † † †

* Shortened infection

† Transitory infection

‡ No infection visible

It will be noted that when blood containing *P. cynomolgi* is inoculated into monkeys immune to this species, usually no visible parasites appear, they are very scanty and persist for a few days. Sporozoite infections are no more effective.

* Strain originally came from the
New York

of Ind

the Rockefeller Foundation,

RESULTS OF INOCULATING *PLASMODIUM GONDERI** INTO MONKEYS IMMUNIZED AGAINST *PLASMODIUM CYNOMOLGI*

Fifteen mls of blood were withdrawn from a rhesus monkey which had a chronic infection of *P. gonderi*. The blood was citrated and was divided into five equal portions, each containing about 250 000 parasites. These were inoculated into four immune monkeys (Table I) and into one control (M 152). The course of the ensuing infections was studied in daily blood films, and the density of parasitaemia is shown in Table II. Unfortunately, the control monkey died after 11 days, but the normal course of this infection in *M. mulatta* is sufficiently well known for us to be able to predict what would have happened in the control monkey had it lived, that is to say—a chronic infection would have developed and persisted for years.

TABLE II

Course of parasitemia of P. gonderi in cynomolgi immune monkeys
Number of parasites per 10,000 erythrocytes

Days after infection	Monkey number				
	Control 152	81	99	101	102
1	-ve	ve	-ve	-ve	-ve
2	+ve	+ve	-ve	-ve	-ve
3	+ve	+ve	+ve	+ve	-ve
4	+ve	+ve	+ve	+ve	-ve
5	6	1	1	-ve	-ve
6	8	6	+ve	-ve	-ve
7	18	7	8	+ve	+ve
8	45	43	15	1	+ve
9	116	87	37	2	1
10	*74	327	100	8	4
11	Died	444	71	24	10
12		1*1	73	68	*9
13		41	31	56	124
14		19	12	34	146
15		20	12	12	182
16		16	13	0	105
17		36	11	18	35
18		43	7	*1	5
19		77	2	25	1
20					
21		60	4	*3	8
22		47	3	9	8
23		33	2	6	13
24		14	1	6	35
25		16	3	15	28
26		17	1	25	52
27					
28		14	+ve	31	24
29		11	+ve	23	34
30		17	+ve	36	23
31		51	+ve	11	38

*Strain obtained from the School of Tropical Medicine, Antwerp

cross immunity between two organisms must mean the possession of a common antigen, its absence the lack of one indicating a fundamental difference which may be specific in character. The absence of cross immunity alone would have little diagnostic value, but when associated with other evidence might provide useful confirmation of the status of a parasite. Our experiments suggest that there is no cross immunity between *P. cynomolgi* and *P. gonderi* in rhesus monkeys confirming that they are two distinct species. Table III presents the characters which may be used to differentiate these two species.

TABLE III

Differential characters of Plasmodium cynomolgi and Plasmodium gonderi

Character	<i>P. cynomolgi</i>	<i>P. gonderi</i>
Origin	East Indies	West Africa
Host (Vertebrate nature)	<i>Macaca mus</i>	<i>Cercopithecus</i> spp.
Host (Insect laboratory)	<i>A. maculipennis</i> -excellent	<i>A. maculipennis</i> poor
Course of infection in rhesus	Self limiting	High chronic parasitaemia
Time of rupture of schizonts	Early morning	Late afternoon
Cross immunity	No	No
Effect on erythrocyte	Distinct enlargement	Slight enlargement
Double chromatin dots	10 per cent in young rings	Rare or absent
Number of merozoites	15-4	12

Both species have a 48 hour blood cycle, produce Schuffner's dots, show double invasion of red blood cells, exhibit indistinguishable gametocytes and have sporozoites of equal length (11.5μ dried).

SUMMARY

1. Monkeys immunized against *P. cynomolgi* are susceptible to *P. gonderi*.
2. A monkey cured of a long standing infection of *P. gonderi* proved to be susceptible to *P. cynomolgi*.
3. This absence of cross immunity plus other evidence indicates that the two species are distinct from each other, though both belong to the 'benign tertian malaria' group.

260 *Absence of Cross-Immunity Between P. cynomolgi and P. gonderi*

REFERENCES.

- DRAPER, C. C (1953)
 FONSECA, F da (1951)
 JEFFERY, G M, WILCOX, A and YOUNG, M D (1955)
 MAYER, M (1907)
 MULLIGAN, H W (1930)
 REDMOND, W B (1930)
 RODHAIN, J (1954)
 RODHAIN, J and VAN DEN BERGHE, L (1936)
 RODHAIN, J and VAN HOOF, T (1940)
 SIMTON, J A and MULLIGAN, H W (1933)
- Parasitology*, **43**, p 130
Mem Inst Oswaldo Cruz, **49**, p 543
Trans Roy Soc Trop Med Hyg, **49**, p 166
Med Klin, **3**, p 570
Arch Protistenk, **84**, p 285
J Infect Dis, **64**, p 273
Indian J Malar, **3**, p 369
Ann Soc Belge Med Trop, **16**, p 521
Bull Soc Path Exot, **33**, p 107
Rec Mal Suro Ind, **3**, p 381

A NEW APPROACH TO THE EPIDEMIOLOGY OF MALARIA

BY

G MACDONALD, CMG, MD, FRCP, DPH, DTM

(Director, Ross Institute of Tropical Hygiene, London)

(September 5 1955)

OUR knowledge of the epidemiology of malaria owes more to workers in India than in any other country of the world. It was first advanced by Dempster (1848) who established the general circumstances in which malaria occurred, the means by which it could be accurately measured and some of the means by which it could be prevented. The transmission of the disease by mosquitoes, the differing vectorial capacity of anopheline species, the causation and nature of epidemics and the nature of hyperendemic malaria were all described in India as the highlights of a mass of work which has no comparison elsewhere. Before 1929 this was distributed in a number of journals but since then has been for the most part collected in one series which is worthy of the work which it records.

The author owes much to the example of workers on malaria in India, to the experience he has had there and to the example of workers on malaria in India with that elsewhere. The understanding of Types of malaria

1950a b, 1952a b, 1953, 1955) which though essentially simple in themselves are partly written in a language unfamiliar to most malarialogists, of mathematics. The object of the present paper is to translate much of this working attempt to expose the methods of work used and show how the products of mathematical analysis can be used to elaborate understanding of the normal epidemiology of malaria in the field.

FACTORS INVOLVED

The state of parasitæmia is an intermittent one varying in length with characteristics of the parasite and the immunity of the individual concerned. Proper account can be taken of these variations but it is convenient to consider happenings in a totally non immune person in whom it has been shown that *Plasmodium falciparum* infection may typically be patent on about 200 to 250 days whilst gametocytes may be present on about 80 days following a single infection. On each of these days the patient may be bitten by vector mosquitoes let us say in illustration by about 10 and if the infection is established it proceeds through oocyst development to the production of sporozoites. Figure 1 shows the approximate speeds of development of *P. falciparum* and *P. vivax* in the mosquito to the stage of production of sporozoites. In ordinary tropical climates one might say that the normal time of development of *P. falciparum* is 12 days, though this may be much prolonged in cooler weather. The proportion of mosquitoes which survive sufficiently long for this development depends on the mortality to which they are exposed. Figure 2 shows how this varies with mortality. Circumstances in which the daily mortality is ten per cent—a not unreasonable figure—may be used in illustration, in which case about 30 per cent will survive for this period.

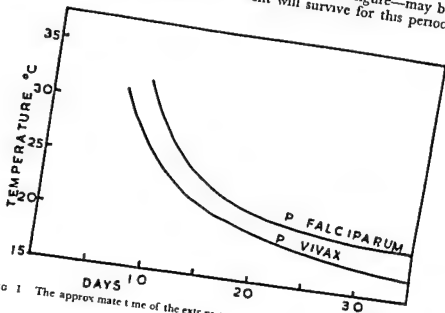


FIG. 1. The approximate time of the extrinsic cycle in relation to temperature.

Next comes the question of how long the mosquito may be expected to survive to bite other people should it have lived long enough for the development of sporozoites. Again it depends on the mortality to which the mosquitoes are exposed and is illustrated in Figure 3. In the example chosen with a 10 per cent mortality the expectation of such life would be about ten days. The number of

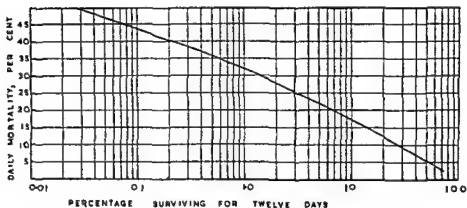


FIG. 2 The effect of mosquito mortality on survival through the extrinsic cycle

people whom the mosquito will bite during that period depends on its biting habit, under tropical conditions the majority of anophelines take a blood meal once in every two days but their habit of selection of man or other animal varies very greatly. In some, for instance *A. gambiae*, the meal is almost invariably on man, in others, the meal is rarely on man if other foods are available. In the example used for illustration it may be taken that it feeds normally on man and once in every two days, the development of the parasite takes place in the mosquito, which it thus transfers to a new individual, but the period of development which can be taken as ten days, and in the case of *falciparum* infections by a further ten days before gametocytes appear and the case becomes infective to mosquitoes.

CONCEPTS

In the example chosen the individual was bitten on each of 80 nights by ten mosquitoes of which 30 per cent survived for the development of sporozoites, and each of which took five subsequent feeds. There is a potential infection of as many as 1,200 people from the original case. This introduces the idea of a reproduction rate, the number of secondary cases which potentially could be infected

eventually restrain it. In the case of insect borne diseases there are two brakes, one is the existence of previous infections in the individuals who receive infective bites, so that the subsequent bites are non effective and do not actually produce new cases of the disease. The other brake is the occurrence of superinfection in the mosquito, which may have a previous infection so that a second infection does

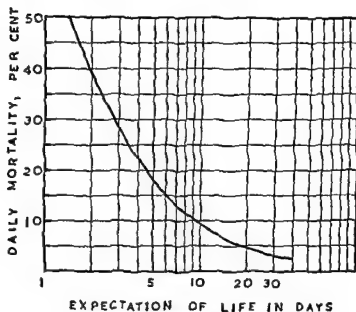


FIG. 3 The effect of mortality on expectation of life

not materially increase its infectivity. These factors together reduce the gross reproduction rate to a net one which may be much lower. Should this fall below one, successive generations of cases will be smaller than their predecessors and the disease will disappear, should it be greater than one, successive generations will increase and the disease will mount in the population. Obviously the objective of all control is to keep the reproduction rate below one so that successive generations decrease in size and the disease disappears. Since in the last resort when it is in process of disappearing, the gross and net reproduction rates are the same it can be said from the start that the objective is to reduce the gross reproduction rate below one.

The idea of a critical level is also introduced here. It is not necessary to eliminate transmission completely in order to get disappearance of the disease but only to reduce it below some significant level, after which the disease will decrease indefinitely. This is a most important concept in general epidemiology and particularly in that of malaria, and explains the occurrence in some parts of the world of anophelism without malaria, the transmission being at such a low rate that the disease automatically extinguishes itself.

INTERACTION OF FACTORS

Fundamental epidemiology considers this cycle of transmission in various stages. The sporozoite rate depends on the number of gametocyte carriers in the population, on the period of the extrinsic cycle and on the mortality rate of the mosquitoes in a manner illustrated in Figure 4. The mortality is here put as a survival

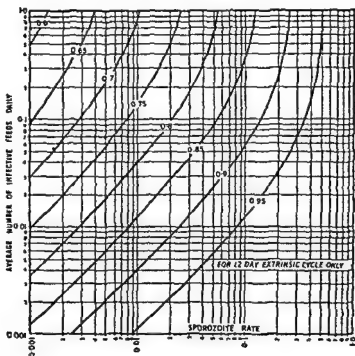


Fig. 4. — A series of graphs showing the sporozoite rate corresponding to given frequencies of infective feeds. Each graph refers to a different probability of survival which is shown on the line. The frequency of infective feeds is the product of the frequency of biting man and the infective gametocyte rate.

rate, a 95 meaning that 95 per cent survive through one day. The graphs have

infective person on any particular day, for in these conditions in Africa the prevalence of infective people is reduced by the occurrence of immunity. In parts of India where malaria is transmitted by *A. culicifacies* very much lower sporozoite rates of the order of 0.1 per cent are often recorded. In an extensive series of surveys made by Russell and his co-workers in Madras it was 0.064 per cent; this was attributable to a 22.5 per cent daily mortality of the mosquito which took only, on the average, 1 out of 40 of its feeds on man, an extrinsic cycle for *P. vivax* of about nine days, and a gametocyte rate in the population of about 13 per cent.

starting with an original abrupt step, followed by a pause, and after a lag by a second more rounded curve.

Epidemics in nature are almost always mixed ones of *P. vivax* and *P. falciparum*, and the fact that immunity to *P. vivax* alters the timing together form a combined compared with actual, long epidemics of 1934/35,

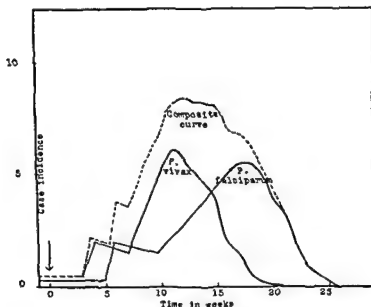


FIG. 6. Two synthetic epidemic curves built on identical data except for differences in incubation interval and extrinsic development, corresponding to those of *P. vivax* and *P. falciparum*.

and in most subsequent ones, one can trace the same general form. All natural epidemics do in fact consist of two separate curves as has been shown, and the occurrence of a very abrupt start, the preliminary appearance of *P. vivax* and the features. of Ceylon multiplication

tion of mosquitoes necessary to produce such a catastrophe.

Epidemic curves reflect the admission of new cases but there are two factors new cases and the parasite rate. The latter mounts from the start of the epidemic to achieve a plateau, which may be 100 per cent of the population or less. In analysis it is represented by a theoretical formula which cannot be directly checked in nature, because when this steady stage is reached immunity sets in, alters the value of one of the factors involved—the duration of the disease—and invalidates

direct comparison. The expression might, therefore, remain one of theoretical academic interest except that it can be used in subsequent examination of the stability of equilibrium, a very important concept which may be illustrated by a mechanical analogy: no engine however well governed runs perpetually at the same speed, some increase of the load on it produces some slight decrease in speed though this may later be adjusted by the governing mechanism. Now imagine two engines one of which is fitted with a reasonably efficient governor which maintains it running at roughly the same speed whatever the load that may be put upon it, and another which has an extremely inefficient governor so that with variation of

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overlap of infections in the mosquito and the more efficient the governing mechanism, resulting in a much more stable epidemiological condition with less tendency to vary from the mean. It is in exactly this characteristic of degree of

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several years. However, in other places and notably in northern India, parts of Pakistan and in Ceylon, the variations from year to year are extreme. In some there is a periodic variation with a cycle of about eight years, but apart from this good and bad years follow each other in an irregular manner. Examination of the vectors of malaria shows that these two types do in fact depend on the longevity and the biting habit of the mosquito as theory had indicated they would.

EPIDEMIOLOGICAL TYPES

By this route the concept of two quite different types of malaria, stable and unstable, is introduced. The first is caused by transmission by a mosquito which feeds often on man and has good prospects of life. The critical level is extremely low and in consequence anophelism without malaria is extremely rare. The disease shows little tendency to fluctuate from its normal, and epidemics amongst the indigenous inhabitants are rare. In consequence of the regular transmission of the disease immunity is fairly readily established amongst the local population, adults often show a firm resistance to it, and the disease is very difficult to control by anti-larval measures and relatively difficult by magicial measures. On the

stable malaria caused by transmission by a short lived vector
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greatly from year to year, sometimes with dramatic epidemics of extreme severity

as those in Ceylon and the Punjab. The irregularity of transmission and the occurrence of consecutive years when it happens only on a small scale, results in a poor stimulus to the development of a firm immunity in a population.

These processes can show what is happening in epidemiology and why it is happening, why malaria is so vastly different in, for instance, central Africa where it is of the extreme stable type, and in Ceylon and the plains of India where it is of the extremely unstable type, one can in fact map out in the world zones where the epidemiological types differ. In northern Europe, for instance, malaria was relatively unstable, and is in fact in process of natural control by deviation of anophelines from man, whereas in southern Europe it is of the extremely stable type and remained unchanged until the development of magistral control in recent years.

CONTROL

The object of all control is to reduce the reproduction rate below one. Without suggesting that the rate should be accurately calculated in every region, one should at least form a concept of the nature of the reproduction rates and the degree of reduction necessary to establish control of the disease. Theoretical examination can show the changes in the density of anophelines, in their daily

and longevity of the local vector, from them to determine the actual amount of transmission and the potential amount should the entire population be non-immune, in the form of the basic reproduction rate, from these, estimates must be made of the changes in conditions necessary for control. It is then for the executive to determine how these changes can best be produced, though in most cases it will be by the use of residual insecticides. The determination of the actual mortality achieved by the use of particular insecticides in the field, using experimental trap huts, when related to estimates of the mortality necessary can, undoubtedly, avoid wastage.

Though the immediate attack should usually be through insecticides, their

"spontaneous" regressions have occurred in places where the local mosquito is readily deviated from man to cattle, and it seems probable that the regression follows some slight change in agricultural pattern which has led to the more ready availability of animal food. There are large areas in India where even before the application of the modern methods of control, malaria was absent despite the presence of some vector mosquitoes, and there are other considerable areas where the disease has shown itself to be evanescent, coming and going in an irregular way following minor changes in the environment. This indicates that over very large tracts indeed the basic reproduction rate was naturally near its critical level.

of one, and the amount of change needed to bring it permanently below that level would be small. Any deviation of the mosquito from man to animal must act in this direction and the influence of such deviation is very marked. The most interesting epidemiological study in India therefore lies in those areas of anophelism without malaria, and should concern itself with the precise reasons why malaria is absent, and the levels of mosquito prevalence, longevity and anthropophilism which permit the co existence of man and mosquito without the transmission of the disease. With the knowledge gained in such studies the present great malaria control programme could rationally go on to one of elimination throughout the world.

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REFERENCES

- | | |
|------------------------|--|
| DENPSTER, T. E. (1848) | Reprinted in <i>Rec. Mal. Surv. Ind.</i> (1929-1930) |
| | 1, p. 69 |
| MACDONALD, G. (1950a) | <i>Trop. Dis. Bull.</i> , 47, p. 907 |
| Idem (1950b) | <i>Ibid.</i> , 47, p. 915 |
| Idem (1952a) | <i>Ibid.</i> , 49, p. 569 |
| Idem (1952b) | <i>Ibid.</i> , 49, p. 813 |
| Idem (1953) | <i>Ibid.</i> , 50, p. 871 |
| Idem (1955) | <i>Proc. Roy. Soc. Med.</i> , 48, p. 295 |
| ROSS, R. (1916) | <i>Proc. Roy. Soc., Ser. A</i> , 92, p. 204 |

SOME PROBLEMS ON CHEMOTHERAPY OF MALARIA.

BY

LIEUT-COLONEL JASWANT SINGH, M B, Ch B (Edin), D P H (Eng),
D T M & H (London)

(Director, Malaria Institute of India, Delhi)

(September 10 1955)

With the advent of modern synthetic antimalarials, treatment of acute attacks of malaria nowadays presents few difficulties. The most powerful of the series (by oral route), as judged by the speed of action in relieving clinical symptoms as well as by the clearance of asexual parasites from the peripheral circulation, are the drugs of 4-aminoquinoline series. Even in extremely severe cases, parenteral administration of chloroquine preparations has been found to be as effective as quinine though some consider that the former is somewhat better. However, that would need detailed comparative studies against all the available strains of plasmodia before a final conclusion can be drawn.

As a blood schizonticide, neither proguanil nor pyrimethamine is as rapidly active as the 4-aminoquinolines. Besides their comparatively slower action,

Although satisfactory reports on mepacrine have been presented by many workers, that compared to the and that it is likely to though in a very small percentage of cases. In repeated doses quinine acts almost as fast as mepacrine.

Thus the choice of antimalarials for treatment of acute attacks of malaria naturally falls on the 4-aminoquinolines administered orally as a single dose of 0.6 gm (adult) in partially immune population, if the condition is not too serious. Under emergency conditions and in cases where the patient is unconscious or if there is incessant nausea and vomiting, parenteral administration of chloroquine or quinine hydrochloride or dihydrochloride would obviously be called for.

Thus in the discovery of compounds like the 4-aminoquinolines a stage has now reached that perhaps further development of a more potent and rapidly effective remedy for clinical cure may not be necessary in view of rapid reduction of the incidence of malaria on account of large scale control measures

Prima facie it would appear that the main problem in the treatment of malaria has practically been solved. But on deeper consideration, it becomes evident that there are still many lacunæ in our knowledge of the subject. For example, it is not clear why certain drugs like quinine, mepacrine and the 4 aminoquinolines which are such powerful blood schizonticides, yet have no effect on the sporozoites or the tissue forms (primary or secondary) of the plasmodia. Again drugs of the 8 aminoquinolines which are tissue schizonticides, particularly effective against the secondary exoerythrocytic forms, have poor action against the asexual erythrocytic forms, specially in respect of *P. falciparum*. Similarly, ex
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plasmodia. Further, it is also common experience that some strain of a plasmodium is highly susceptible to a particular drug while others are comparatively refractory and need much larger doses. It is also not clearly known as to why should plasmodia develop resistance to certain particular groups of compounds like proguanil or pyrimethamine, and not against drugs like quinine, mepacrine or the 4 aminoquinolines.

Factors like the phases of plasmodium life cycle, somewhat different pattern in the life cycle of *P. vivax* and *P. malariae* as against *P. falciparum* in the human host, the metabolic processes of plasmodia in the tissues like the liver and also in the blood, the chemical constitution of antimalarials and their effect on plasmodium metabolism, metabolites of antimalarials, pharmacological considerations like break down products, absorption and distribution of the drug in the tissues of the host thereby aiding its penetration, and many other problems of similar nature have to be carefully considered.

As to the life cycle of malaria parasites, most of the lacunæ in our knowledge have been filled since the discovery of the tissue phase. Although, it is the general opinion that secondary exo erythrocytic forms develop in *P. vivax* and *P. malariae*, there is reason to believe that such forms are absent in *P. falciparum*. As to why such stages are not developed in the issue. Obviously the behaviouristic. Further, it is well known that certain methamine and the 8 aminoquinolines are effective against the primary tissue phase of this plasmodium but not against the others. Since the rate of absorption, distribution, and tissue concentration of the same drug could not be fundamentally different in the same host, it is difficult to understand as to why there should be such a marked difference in the reaction of plasmodia to these compounds. Naturally, therefore, this leads one to speculate that perhaps the metabolic processes of the pre erythrocytic forms of *P. falciparum* are different from those in respect of *P. vivax* and *P. malariae*. Again it would appear that perhaps similar differences exist in the metabolic processes in the same plasmodium, like *P. vivax* at the primary and secondary exoerythrocytic forms, because 8 aminoquinolines, though active

to be an extension of the sporogony phase of the plasmodium yet drugs which are effective against the tissue phase are totally ineffective against the sporozoites in spite of the somewhat similar cytological character. Since it is believed that antimalarials act by interfering with the enzyme system there is reason to believe that the metabolism of the two stages sporozoites and pre erythrocytic forms are different. This variation perhaps depends on the particular environment where they are usually lodged like the salivary glands or the liver.

There is also the possibility of differences in the metabolic processes of tissue forms and erythrocytic forms firstly because powerful blood schizonticidal drugs like quinine, 4 aminoquinolines etc. are ineffective against the tissue forms of the same plasmodium and secondly powerful tissue schizonticidal drugs like 8 aminoquinolines are poor blood schizonticides. Again it may be noted that most of the existing antimalarials which are powerful blood schizonticides are poor gametocytocidal drugs. On the other hand 8 aminoquinolines which have powerful gametocytocidal action (also tissue schizonticides) are poor blood schizonticides. Could there be differences in the metabolic processes even in the sexual and asexual forms of the same plasmodium? Also could the metabolic pattern of gametocides and tissue forms of the same plasmodium have some degree of similarity?

As to the metabolic processes of malaria parasites and drug action the present day knowledge is limited. Although quinine has been known for centuries to have specific action against malaria parasite it is surprising to note that as yet so little is known as to how it acts. This is true for other antimalarials as well. The earliest workers like Christophers and Fulton (1938) demonstrated that quinine, mepacrine and pamaquin inhibit the oxygen consumption by the parasites. Mepacrine has been shown to interfere with the respiration of malaria parasites but quinine much less so. Silverman *et al* (1944) believe that quinine affects the

pre-erythrocytic forms of *P. gallinaceum* in tissue culture (Ionkin, 1946). According to Hellerman *et al* (1946) atabrin and quinoline bases are enzyme inhibitors. These are likely to combine with certain acidic groups of the enzymes. If such groups combine with co-enzymes a competition is set up between co-enzyme and the inhibitor. Work and Work (1948) believe that this inhibition may not be specific to one enzyme or class of enzymes. According to them 'the danger of misinterpreting the action of an inhibitor as a result of testing on an insufficient number of enzymes is well illustrated in the case of the antimalarial drugs'. Findlay (1951) observes that quinine, mepacrine and pamaquin might interfere with a number of reactions essential for the metabolism of malaria parasites.

Some Problems on Chemotherapy of Malaria.

According to him, "there is still uncertainty as to how far any such inhibition is responsible for antimalarial action". In the same way, there is hardly any indication as to the mode of action of proguanil.

As to the correlation between chemical constitution and antimalarial drug Magdson *et al* (as quoted by Findlay, 1951) suggested that different parts of the molecule of a drug, like mepacrine, have different functions and that basic side chain is primarily of pharmacological importance, controlling absorption and distribution of the drug in the host and aiding its penetration into the parasite, while the substituted acridine or quinoline nucleus is responsible for the plasmodicidal action. But by experience, and from studies on newer antimalarial drugs, it has been observed that it is difficult to establish such correlation. Findlay (1951) observes that "to attempt to correlate chemical constitution and antimalarial action has so far proved an impossible task".

It is also not clearly understood whether a compound exerts its action through the parent or its metabolites. It is known that quinine is degraded the system to a 2-hydroxy derivatives. But this has been found to be inferior quinine (Marshall and Rogers, 1948). Spectrographic study of mepacrine do not indicate acridines as the possible metabolic products. During their studies on pamaquin, Josephson, Taylor *et al* (1951) had observed that concentrates obtained from blood, tissues and droppings of the chickens treated with pamaquin, possessed antimalarial activity *in vitro* equivalent to 16 times that of the parent compound. This activity could not be accounted for on the basis of pamaquin present in these concentrates. But subsequent *in vivo* studies on one of the metabolites isolated by (Josephson, Greenbergh *et al*, 1951) did not show any antimalarial activity (Schmidt, 1951). Elderfield and Smith (1953) were also unable to establish any definite metabolite of pentaquin. Similarly ultraviolet irradiation of 4-amino-7-chloroquine derivatives and study of their breakdown products, did not reveal any new product (Price *et al*, 1948).

Hawking and Perry (1948) suggested that proguanil itself is not active it is converted to an active metabolite. Carrington *et al* (1951) and Crowl and Levi (1953) were able to isolate an active metabolite of proguanil as well as an inactive compound originally isolated by Crounse (1951). The active metabolite is a dihydro triazine derivative but according to Schmidt *et al* (1952), the parent compound was found to be two to four times more active than the metabolite. Subsequently, however, a large number of triazine compounds have been synthesized and some of them have shown high degree of activity against *P. gallinaceum* in chicks.

In view of the points raised above it is apparent that the existing knowledge on the problem of chemotherapy in malaria is still limited. At the moment our primary objective is to develop a suitable compound which in non-toxic doses is highly and equally effective against all the phases of the plasmodial life cycle, or at least against the asexual erythrocytic and sporozoites as well, it should be a powerful blood schizonticide and gametocyticide. If this proves to be a powerful blood schizonticide and gametocyticide, it should be effective against the gametocytes and sporozoites as well, it would be an added advantage. This is particularly necessary in case of *P. vivax* infection for though it is quite easy to effect a clinical cure with the usual antimalarials, its radical cure continues to be a baffling problem. No doubt some of the newer 8-aminoquinolines

possess curative action but there are always the toxic hazards encountered, though in small number of cases.

In order to achieve this objective, it would be essential to understand clearly the metabolic processes of plasmodia at all the phases, particularly the tissue and blood forms. Once the basic requirements of the plasmodia are well understood,

REFERENCES

- CARRINGTON, H C CROWTHER, A F, DAVEY, D G, LEVI A A and ROSE, F L (1931) *Nature* 126, p 1081
- CHAKRAVARTY, N K and CHAUDHURI R N (1933) *J Ind Med Assoc*, 22, p 155
- CHAUDHURI, R N (1934) *Tech Report, Scientific Advisory Board Indian Council of Medical Research*, p 198
- CHRISTOPHERS S R and FELTON, J D (1938) *Ann Trop Med Parasit*, 32, p 43
- CROUNSE, N N (1931) *J Org Chem*, 16, p 492
- CROWTHER, A F and LEVI, A A (1933) *Brit J Pharmacol*, 8, p 93
- CURD, F H S and ROSE, F L (1916) *Nature*, 103, p 707
- EASTFIELD, R C and SMITH L L (1933) *J Amer Chem Soc*, 55, p 40
- FINDLAY, G M. (1931) *Recent advances in chemotherapy*, Vol II, pp 519, 520, 533 J & A Churchill Ltd, London
- HAWKING E and FERRY, W L M (1918) *Brit J Pharmacol*, 3, p 320
- HELLERMAN, L, BOVERNICK, M R and POTTER C C (1916) *Fed Proc*, 5, p 400
- HUFF, C G and COULSTON F (1914) *J Inf Dis*, 75, p 231
- JAMES, S P, NICOL, W D and SHUTE, P G (1931) *Lancet*, II, p 341
- JASWANT SINGH, RAY, A P, MISRA, B G and BASU, P C (1932) *Ind J Med*, 6, p 411
- JOSEPHSON, E S, GREFENBERG J TAYLOR JANE and BASH, H L (1931) *J Pharm Expt Therap*, 103, p 7
- Proc Soc Expt Biol Med, 76, p 700
- J Pharmacol, 75, p 89
- Biochem, J 43, p 411
- J Amer Chem Soc, 70, p 2943
- Unpublished report
- Proc Soc Expt Biol Med, 80, p 167
- J Inf Dis, 73, p 212
- Ind J Med, 7, p 5
- Brit J Pharmacol, 1, p 163
- The basis of chemotherapy Interscience Publishers Inc, New York
- SCHMIDT, L H (1931)
- SCHMIDT, L H, LOO, T L, GRADIN, R and HUGHES, H B (1932)
- SILVERMAN, M, CRITHAM, J, TALLAFERRO, L G and EVANS, E A (Jr) (1944)
- SRIVASTAVA, R S, CHAKRAVARTI, A K and MUKHERJEE, S K. (1933)
- TOXIN, I M (1916)
- WORK, T S and WORK ELIZABETH (1914)

ANOPHELES RESISTANCE IN RELATION TO MALARIA CONTROL PROGRAMME PLANNING

JOHN M HENDERSON, C E *

*(Technical Development Laboratories, Communicable Disease Centre, Public
Health Service, U S Department of Health, Education, and Welfare,
Savannah, Georgia, U S A)*

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INTRODUCTION

THE great expansion in malaria control activities which has taken place within the past ten years with the development of D D T and related residual insecticides has created many new problems and increased the importance of many old ones. In addition to perplexing problems related to the development of effective and adequate malaria control organizations, is the problem of resistance to residual insecticides by anopheline vectors.

The extent to which these issues can be resolved naturally varies with the existing situation in each country, including financial resources, the availability of suitably trained professional personnel, ways of thinking, and competing exigencies. In this connection, the author is reminded of his experience of 25 years ago in a State-wide programme of malaria control in one of the States of the United States of America, in which the situation can be summed up by the following bare facts: Area served—58,000 square miles. Population served—three million. Number of malaria cases—50,000 to 100,000. Number of professional personnel assigned to malaria control—one. Paradoxically, it was not until malaria had largely ceased to be an important socio-economic burden that funds became available for the development of adequate malaria control organizations in this and other malarious States of the United States.

Under such circumstances it was futile to propose new plans for the existing malaria control "organization" to carry out, which invariably required additional trained personnel. Today, throughout the world, malaria control programmes fortunately are staffed somewhat more adequately, but major shortages of key personnel are still all too common. Such shortages understandably impede the adoption of "ideal" plans based on theoretical concepts, some of which may be involved in this article.

*Formerly Professor of Sanitary Science, Columbia University School of Public Health

ANOPHELES RESISTANCE

In considering any matter of insect resistance, two governing natural laws should be recalled to mind. One is that the development of resistance is a product of selection pressure, its duration, and the genetic capacity of the species to develop resistance. The other is that, barring eradication, any species inevitably will develop resistance of one type or another, provided the degree and duration of selection pressure in combination are sufficient to threaten species survival.

When one surveys the results of ten years of global application of the chlornated residual insecticides for agricultural, public health, and pest control purposes the comparative lack of confirmed resistance development in the field among the anophelines is little short of amazing. This is especially true of many of the more anthropophilic anopheline species which, in some areas, have been bombarded for eight years or longer in specific localities with DDT residual house spray. Malaria has been eradicated in extensive subnational areas where the biotic potential of the disease was high, with and without vector eradication, and has been controlled in other far more extensive areas of high biotic potential. Malaria eradication also has been realized in other extensive areas where the disease was not so firmly entrenched. In a few special cases where the vector had not achieved a status of long, indigenous adaptation, species eradication was even achieved as a partly unexpected dividend from malaria control operations. Yet, so far, only four of about 50 significant anopheline vector species are considered to have acquired physiologic resistance in local or more extensive areas. These are *Anopheles sundacus* in Indonesia, *A. maculipennis*, *A. sacharovi*, and *A. superpictus* in Greece, and *A. sacharovi* again in Lebanon (Pampana, 1954; Garrett-Jones, 1954; and Crandall, 1954-1955). With the exception of Lebanon, physiologic resistance development has occurred in the presence of adulticidal treatments *cum* larviciding, although these selection pressures were not necessarily applied continuously and concurrently. Even in Lebanon, the possibility of larval exposure incidental to agricultural insecticiding cannot be ruled out. Earlier reports of resistance in *Anopheles quadrimaculatus* in the T V A area of the United States of America have not been substantiated (Hawkins and Hall, 1954). The species is under larvicidal treatment in this area, but such treatment is restricted to federally-owned properties bordered by private lands.

Behaviouristic resistance as a developmental factor cannot be as readily evaluated nor, as pointed out by others, is it necessarily adverse to man's interest. It is intended to deal both to anophelines which do not normally enter or those possessing hyper-irritability. It is at times difficult to determine whether observed behaviouristic resistance was a pre-existing characteristic of the dominant population group, of an important biotype fraction which has not increased in prevalence, or whether the resistant biotype has become more prevalent as a result of the selection process. An example of behaviouristic resistance which has impeded malaria control is provided by *A. sergenti* and *A. superpictus* in the Jordan Valley (Farid, 1954). One which has not prevented malaria control is that of *A. albimanus* in Panama (Trapido, 1952-1954).

Compared with the house fly, this relatively favourable state of affairs reflects the lower genetic capacity of the genus *Anopheles* to develop resistance, supplemented in some cases by fewer generations per year. The exposure of a smaller fraction of the species population to insecticides is an added possibility. The latter factor highlights the well established principle that residual house spray in malaria control is a highly selective tool which is intended to intercept only that fraction of the species population which is infective to man.

Yet, the importance of anopheline resistance should not be minimized. It is already a problem of major importance in some of the countries or local areas in

spread of anopheline resistance, rather than contending with existing resistance problems.

Efforts which are being made, or might be made, to solve the resistance problem may be divided into two categories: (1) Laboratory studies, and (2) Field operations.

LABORATORY STUDIES

These consist of (1) Basic physiologic, biochemical, and genetic studies on the mechanism of resistance in arthropods, particularly anophelines, and the genetic processes by which physiologic and behavioural resistances are developed, and (2) the development of new insecticides, formulations and techniques of application. The apparent purpose of the basic studies is to permit making more intelligent searches for new insecticides and synergists, but the theoretical implications of such research extend further.

In combination the present main hopes of such studies are in the following directions: with the proviso that any insecticide which satisfies one or more of these objectives must also be relatively safe to man in application and in use, and must be economical in cost.

A Development of an even more effective residual insecticide which will

test results of 70 to 90 per cent tends to be exophilic in resting place with respect to human dwelling places, while the multidentate zoophilic race tends to be endophilic. This hypothesis, accordingly, may not apply in exceptional cases.

B The development of new insecticides with differing periods of residual effectiveness, but which in other respects would have substantially equal merits.

Anopheles Resistance and Malaria Control

By selecting for each area an insecticide having an effective residual life equal to but no greater than, the length of the seasonal period of disease transmission selection pressure during the remainder of the year could be avoided. Such insecticides should have high effectiveness with an abrupt termination point. The merits of this objective are sharply limited by the facts that (1) a high proportion of the number of annual generations of vectorial species in the more malarious area occurs within the malaria transmission season, (2) variation in length of effective life can be achieved with existing insecticides to a considerable extent by choosing between available insecticides and by selection of dosage rate, and (3) it is not operationally feasible for residual spray crews to apply insecticide to all houses at the optimum moment—several months may be required for a spray crew to cover its territory with a single application.

C The discovery and development of new insecticides formulations, and techniques of application by both haphazard and systematic methods. The development of very high resistances and cross resistances to many of the newer insecticides by arthropods of agricultural or public health importance has generated what appears to be a perpetual race between man and insect in insecticide development. Although centered mainly on agricultural insect problems, the control of the house fly and various culicine mosquito species also provides important motivation in the quest for new insecticides. In a mosquito abatement district in the State of California in the United States, for example, the entire list of chlorinated hydrocarbon insecticides was thrown into the discard three years ago due to mounting resistance by *Culex tarsalis* and *Aedes nigromaculis* (Geib, 1952). Since then, a number of organic phosphorus compounds have been resorted to this larviciding programme.

Such further new developmental work possesses somewhat less direct significance in malaria control, in view of the slow rate of resistance development in anophelines to residual adulticidal treatments the apparent absence of total spectrum cross resistance in them, and the present availability of one or more acceptable alternative residual insecticides in the chlorinated hydrocarbon group. But there is always the possibility that a new insecticide may evolve which is more effective or more economical, and yet safe for extensive indoor application.

FIELD OPERATIONS

The foregoing laboratory studies have significant potential value in malaria control and eradication, and should be pursued. But it is of great importance that the management of malaria control operations in the interest of avoiding resistance not be neglected in any particular. In a large scale programme even minor operational changes may be difficult or slow to execute, and may temporarily impede operational efficiency and the accomplishment of other urgent objectives. Programme decentralization, although desirable in many respects, may complicate the acceptance and adoption of such changes. The achievement of effective malaria control under adverse operational conditions often is an exacting and difficult task at best. In spite of such obstacles, consideration of the resistance problem in programme planning and execution is essential.

Differences undoubtedly exist in the genetic capacities of different *Anopheles* species to develop resistance, and in the actual resistance of different species, biotypes and even individuals. However, the main variables within this genus in the selection pressure—duration—genetic capacity—equation are considered to be selection pressure and its duration. Certainly this is the case when the house fly is used as a plane of reference. Were it not so early, extremely high resistance would have appeared many years ago in those of the more anthropophilic species which also had genetic potentialities materially higher than the mean level for the genus.

While the degree of selection pressure exerted is very importantly affected by behaviour of the adult anopheline, it is otherwise a controllable variable. Duration of pressure is totally controllable aside from the inherent characteristics of the insecticide employed. Even these characteristics can be modified by varying application rates and practices.

The present main trend of thought in certain malariological circles is to achieve the eradication of malaria as rapidly as possible, and in as large areas as possible, in order to permit the interruption or termination of residual house spraying. Avoidance of resistance is only one element in the total motivation and justification for this concept, but it is a carefully considered factor.

It may be postulated that the optimal condition favouring *Anopheles* resistance development which would be encountered in the field is that of moderately high selection pressure applied perpetually. The degree of pressure would be as high as possible without eradicating the biotype, species, or parasite. In theory, departure in either direction from this optimal selection pressure should reduce the rate of resistance development or totally avoid it.

It is generally considered that even very low selection pressures continued long enough will result in some resistance. There is no doubt this is true of isolated populations, the case of many of the more zoophilic unexposed populations. *Anopheles albimanus* houses at dusk or after dark, dispersing within the night or at dawn to concealed outdoor daytime resting places. Precipitin tests for human blood in this species are commonly below five per cent. Assuming the figure of five per cent to roughly represent the percentage of the population which becomes exposed to DDT. Residual spray within houses in obtaining a single blood meal, that the percentage of survivors from this exposure is not over 20 per cent (or one per cent of the total population), and that this one per cent is then diluted 95 fold by zoophilic feeders in the perpetuation of the local species population, it is apparent that the degree of selection pressure would be negligible. While this example is deliberately oversimplified, it illustrates the principle of population dilution in combination with low selection pressure on the local species population.

However, avoidance of *Anopheles* resistance is not an end unto itself, nor is it an overruling consideration in most areas at the present time. For this reason, overall objectives are best served by increasing the intensity of selection pressure as a calculated risk in order to achieve more rapid malaria eradication and to terminate residual spraying.

Malaria control and malaria eradication have much in common, but differ in important particulars from a programme design standpoint. Both concepts demand in principle a high order of operational competency in the malaria control

Nation wide
surprises which
national interests—

medical, engineering, and entomological—and the utmost in teamwork

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profession is basically the epidemiological observation of the disease in man and, traditionally in many areas, over all command of programme

Globally, programmes for malaria control *per se* may be considered as having conformed to two main patterns. The more common programme has followed the concept of prompt, effective suppression in project areas where operations were carried on. The other pattern, dictated by limitations of supplies and equipment in relation to magnitude of problem, has been aimed at controlling the greatest number of cases of malaria with available resources. By use of relatively high D D T dosage rates, coupled with an optimal frequency of application, malaria transmission in the first pattern might, for example, be reduced 80 per cent in the first year. In the second pattern, the same quantity of D D T might be spread over twice as many houses with the expectation of reducing malaria transmission by only 60 per cent, but among twice as many people. Although the objective of the second pattern is praiseworthy, and was no doubt fully justified a number of years before the threat of resistance became apparent, careful re-examination is warranted if such programmes still exist.

As with species eradication, malaria eradication is directly dependent upon eliminating the last surviving reproduction source, in this case the gametocyte carrier, from each 'useful unit' area. This is the major point of difference between malaria control and malaria eradication. In consequence, malaria eradication, in principle, demands a higher order of programme effectiveness, as previously mentioned. It also demands the regrouping and extension of project areas along different lines than with malaria control programmes. Generally, malaria control and malaria eradication operations should be initiated in areas

greatest number of cases at the lowest cost, be to lower malaria rates to parity with adjoining less malarious areas. Having achieved this parity, however, the project area in a malaria eradication programme should be expanded as rapidly as possible toward inclusion of the total malarious territory comprising the trading area. Since such territories generally conform to transportation routes, they are likely to be irregular in shape. Expansion into areas of low endemicity within such a territory would have priority over initiating work in a new, more malarious, but remote area.

The absolute prevention of reintroduction of malaria into a clean area is, of course not to be expected until national, regional, or even hemispheric and global eradication has been achieved in all areas from which travellers may originate. The goal is rather to reduce the frequency of reintroduction to such a low level that the prospects of restoring large scale malaria transmission and the burden of malaria surveillance are minimized.

In the interest of reducing the hazard of resistance development, as well as economy of effort, many short cuts in finally terminating residual spraying in an area may be postulated. Certainly, continuation of full scale spraying in a district of say, a million people, until several years after the termination of

adequacy of malarialogic services. There is almost certain to be an acute shortage in the quantity of such service which might ideally be desired in every country where malaria is a primary public health problem. Thus, rather than creating a problem of technological unemployment among malarialogists, DDT potentially has created a far greater need than ever before existed.

should antedate residual house spraying.

The first measure is the determination of prevailing resistance baselines for each vector species at judiciously selected observation posts and recurrent testing of the resistance level. At least two published objective tests have been developed for this purpose (Expert Committee on Malaria World Health Organization 1954 and Fay *et al.*, 1953). Such testing is underway but should be far more extensive. When resistance is detected on operating projects by less sensitive methods, it is often too late. Diagnosis is never a substitute for cure, but is an essential prerequisite.

The second measure is the careful restriction of use of chlorinated hydrocarbon insecticides for anopheline larviciding. The circumstances under which the World Health Organization Expert Committee on Malaria has indicated such larviciding should be practised, do not preclude the development of resistance, but do tend to limit its occurrence to restricted geographical areas.

Instances in which larviciding for malaria control should be the method of choice over residual house spraying on economic grounds consist mainly of urban areas or small breeding surfaces in isolated communities such as oases. Larviciding on biological grounds also has been advocated for the control of important exophilic vectors, as is reported to be the case with *A. superpictus* and *A. sergenti* in the Jordan Valley (Farid 1954). Justification for larviciding *cum* residual house spraying would be more often encountered in suburban areas where the joint control of anophelines and certain other mosquito species are involved, but also can be visualized in exceptional situations where malaria is primarily transmitted by an endophilic species and secondarily, by an exophilic species. In the latter case, differences in breeding habitat and adult behaviour might result in the selective exposure of each species.

The importance of avoiding use of the same chlorinated hydrocarbon insecticide against the immature and adult stages of the same anopheline species at the same time and place has been stressed by others. Under such circumstances use of two chlorinated hydrocarbon insecticides which are not closely related has been suggested. However, the extremely high resistances (up to 1300 fold) (Geib, 1955) to a variety of chlorinated hydrocarbon insecticides which have developed in the United States of *A. triseriatus*, *C. tarsalis*, *Aedes taeniorhynchus*, *A. quinquefasciatus*, and *A. albopictus* are larvicides are the extremely high degree of selection pressure. With this in mind, one might say that as long as the patient took cyanide (i.e., larviciding) it matters little whether he also took some other relatively innocuous poison (i.e., adulticiding) at the same time. It also poses the question whether the intensive use of chlorinated hydrocarbon larvicides on an extensive scale is ever warranted for malaria control, even with exophilic vectors. Except where a high degree of sexual isolation exists, it may be postulated that resistance developing in a localized area will be rapidly dissipated by dilution upon interruption of selection pressure, but such development over a large area gives cause for much concern.

The third measure is to pay attention to control of cause as well as control of effect. Malaria eradication is one method of control of cause. Another is the elimination of anopheline breeding places and prevention of the establishment of new breeding places by man. The need for keeping in mind the more traditional methods of malaria control and of avoiding excessive preoccupation with the newer forms of insecticidal work has been pointed out by others (World Health Organization Expert Committee on Malaria, 1954). Yet, it is generally acknowledged that many of these measures are not susceptible of either near term adoption or of widespread adoption over the vast rural areas of the world which form the stronghold of malaria.

However, in many countries, the predominance of man made over natural vector breeding places throughout large areas, is apparent. This is particularly the case in India and many other tropical countries with their vast numbers of roadside borrowpits and of brick pits and their extensive irrigated acreages. The elimination of existing breeding places in these categories would be a gigantic undertaking, and even the prevention of new ones is no easy matter, especially where changes in cultural practices are required.

On the other hand, corrective practices in new undertakings which in themselves yield direct economic benefit (e.g., water conservation in certain irrigation projects), or can be performed at nominal cost incidental to construction (e.g., connecting shallow hillside borrowpits), are the most economical of all malaria control practices. The important consideration which has been given to these problems by some malanologists in India is noteworthy.

The fourth measure is further experimentation with each vector species in the field with respect to dosage rate and frequency of application of residual house sprays. Early field trials of this nature were made in a number of areas in the 1940s. However, they were focused on the interruption of malaria transmission as the main criterion rather than in combination with evaluating selection pressure.

In countries where they are not already underway, the carrying out of further limited experimental studies in conjunction with local operating projects might well be undertaken in order to jointly evaluate malaria reduction and resistance development. Would it not be desirable to deliberately attempt to induce resistance in each important vector in the smallest feasible area, in order to establish a safety factor for general programme operations or to disprove the possibility of resistance development in a particular species under the conditions of such a programme? The length of time needed to carry this through might, of course, be an important weakness.

Would it not be desirable similarly to carry on other limited experimental studies in conjunction with local operating projects which would employ different dosage rates and frequencies of treatment than those conventionally used? Intensification of selection pressure on the general programme in lieu of its reduction might well be in order if the margin of safety is ample and malaria eradication could be expedited by so doing. On the other hand present pressures in some

In consequence, such experiments must be standardized as much as possible and carefully evaluated. No doubt, experiments along these general lines are being undertaken in some areas but are they being undertaken even to the minimum extent necessary in all indicated countries?

SUMMARY

The problem and possible solution of *Anopheles* resistance threats are considered from the standpoints of laboratory research and field operations. The development of resistance is a product of selection pressure, its duration, and the genetic capacity of the species to develop resistance. Any species inevitably will develop resistance of one type or another provided the degree and duration of selection pressure in combination are sufficient to threaten species survival. The slowness of anophelines to develop resistance to insecticides is commented on.

Three end purposes of laboratory studies concerned with *Anopheles* resistance are described. Adjustment of operating practices in the field is advocated in the interest of avoiding resistance problems. Principles underlying the variation of selection pressure and duration of pressure in field practices and programme design are discussed. Brief mention is made of the role of certain traditional methods of malaria control and of the malaria control organization.

REFERENCES

CRANDALL H. A. (1954)

Idem (1953)

EXPERT COM. ON MALARIA WLD HLTH ORG
(1954)

Idem (1954)

Resistance of *Anopheles stephensi* to DDT. A
preliminary report. *Mosquito News* 14, 4
pp. 194-195.

Personal communication.

Fifth Report Annex 3. *Wld Hlth Org Tech
Report Series* No. 60, 47 pp. (Attributed
to Burvine J. and Nash R.)
Main Text.

FARID, M A (1954)

Ineffectiveness of D D T residual spraying in stopping malaria transmission in the Jordan Valley *Bull Wild Hlth Org*, 11, 45 pp 785 783

FAY, R W, KILPATRICK, J W, CROWELL, R L and QUARTERMAN, K D (1953)

A method for field detection of adult mosquito resistance to D D T residues *Bull Wild Hlth Org*, 9, pp 345 351

FIFTH REPORT—EXPERT COMMITTEE ON MALARIA (1954)

GARRETT JONES, C (1954)

Wild Hlth Org Tech Rep Ser, 80, pp 1-42
Evidence of the development of resistance to D D T

GEIB, A F (1955)

HAWKINS, W B and HALL T F (1954)

Presentation—Second Annual Meeting Entomological Soc of America

HOLSTEIN M H (1954)

Biology of *Anopheles gambiae* *Wild Hlth Org*

PAMPANA, E J (1954)

Monograph Series No 9, 172 pp

TRAPIDO, H (1952)

Idem (1954)

SPOROLOGY CYCLE OF MALARIA PARASITES IN RESISTANT AND NON-RESISTANT STRAINS OF MOSQUITOES AFTER EXPOSURE TO DDT

BY

BADRI NATH MOHAN

(Insecticide and Mosquito Repellent Enquiry Indian Council of Medical Research,
Malaria Institute of India)

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INTRODUCTION

In a previous communication it was reported that in *A. fluviatilis* and *A. stephensi* (type) a sublethal contact with DDT did not inhibit the development of eggs whether the females were exposed to the insecticide before or after blood feed or as half gravids (Mohan, 1955). There was close correlation between fertilization and maturation of ovaries irrespective of the exposure to DDT. Fertilized females of both the species showed a significantly higher percentage of mature ovaries than the unfertilized females. It was also observed that exposure to DDT affected a fair number of gravid *A. fluviatilis* and *A. stephensi* in that the eggs were laid at random although suitable water for oviposition was available. The present studies were undertaken to find out the effect, if any, of lethal and sublethal contact with DDT on malaria parasites in resistant and non-resistant strains of mosquitoes, respectively. The effect on *P. gallinaceum* of DDT orally fed to infected fowls as measured by sporozoite infection in *Aedes aegypti* was also investigated.

MATERIALS

The host and parasite species used were a DDT-resistant and a non-resistant strain of *C. fahgens* for *P. relictum* in local sparrows, a DDT-resistant and a non-resistant strain of *A. fluviatilis* for human malaria and only a non-resistant strain of *Aedes aegypti* for *P. gallinaceum* in domestic fowls. All these strains of mosquitoes were furnished by the laboratory colonies.

D D T-resistant strains of *C fatigans* and *A fluviatilis* —While a fuller account of the development of the resistant strains of *C fatigans* and *A fluviatilis* will be published in due course, a few relevant details concerning each species are given below

C fatigans —Both the resistant and non resistant strains of *C fatigans* originated from the same single raft of eggs laid by a wild caught female. Signs of resistance* to D D T first became apparent in the fourteenth generation as a result of the exposure of the adults males and females, to sublethal doses of D D T at each successive generation. In the subsequent generations, there was some progressive increase in resistance which had reached a high level at the time of conducting the experiments with mosquitoes of the forty-third and forty-fourth generations. A brief resume of some of the salient points about D D T resistant *C fatigans* may be relevant at this juncture

While the non resistant strain of *C fatigans* evidenced 100 per cent mortality on being exposed to 200 mg of D D T per sq ft for one hour, the resistant strain showed little or no mortality on being subjected to similar treatment under identical conditions. Adults of the latter strain were resistant not only to mortality but also to the paralysing effect of D D T. The resistant strain showed striking variations in its resistance to D D T. With the dosage remaining the same, some individuals in a given batch of females of the same generation, died after six hours of exposure, others after 12 hours, while still a few others required even more than 18 hours of exposure to die.

A fluviatilis —Similar efforts were made to raise a D D T-resistant strain of *A fluviatilis*. Feeble resistance† was first evidenced in the twenty-ninth generation. There was slight increase in the subsequent generations but the level of resistance still remained low in mosquitoes of the forty-seventh generation which were used in the experiments. In this susceptible species, resistance was very late in appearance and equally very slow in building up.

DEVELOPMENT OF SPOROLOGY CYCLE OF *P RELICTUM* IN RESISTANT AND NON-RESISTANT STRAINS OF *C FATIGANS* AFTER EXPOSURE TO D D T

In all, four experiments were carried out. Resistant *C fatigans* used in the first experiment were of the forty-third generation and in the subsequent three experiments of the forty-fourth generation.

Experiment 1 —Females of the resistant strain of *C fatigans* and of the non resistant strain were kept in separate cages and given an opportunity to feed on the same gametocyte carrying sparrow, the latter during the first half of the night and the former during the second half. Mosquitoes of each strain which had become fully engorged were, in p. of D D T per sq ft for 40 minutes and the second on the third day of 1

* Ind an Council of Medical Research Technical Report of the Scientific Advisory Board for the year 1952, New Delhi p 12

† Indian Council of Medical Research Technical Report of the Scientific Advisory Board for the year 1954, New Delhi p 7

the effect of these exposures was timed to coincide with the early stages of development of the parasite in the mosquito host. Some blood fed females of each strain which were not exposed to DDT were kept for comparison. There were thus t and two of the non resistant strain, parison) insects. They were kept in fed on ten per cent glucose solution o separate exposures to DDT was s whereas it was heavy in the non resistant strain. In spite of a much higher proportion of the latter exposed to DDT, only a few were left alive for dissection. All the groups of mosquitoes were dissected on the same day particularly for the determination of sporozoite infection of the salivary glands after the normal incubation period.

Experiment 2—Each group of the resistant and non resistant strain was given four exposures, the first immediately after infecting blood meal during the night and the subsequent three on alternate days. The dosage of DDT was 200 mg per sq ft in all the cases and the period of contact was 40 minutes for each strain in the first exposure but in the subsequent exposures it was increased to one hour in the case of the resistant strain and decreased to 20 minutes in the non resistant strain so as to get a fair number of the mosquitoes for dissection after the incubation period of the parasite in the mosquito.

Experiment 3—Resistant females which had fed on a naturally infected sparrow were exposed to DDT as above for one hour once daily for the first four days. Some mosquitoes of the same stock which had fed on the same sparrow were not exposed to DDT but kept for comparison.

Experiment 4—In this experiment 300 resistant *C fatigans* females were first exposed to 200 mg of DDT per sq ft for as long as six hours and then on release, immediately given an opportunity to feed on an infected sparrow, during the night. The following morning 24 were up including 14 fully engorged females. All these engorged specimens remained alive until dissection.

Data concerning the foregoing experiments are set out separately in Table I.

The results of comparative infections indicate that mere acquisition of resistance in *C fatigans* was not accompanied by any concomitant change in its susceptibility to infection with *P. relictum*. Both the resistant and non resistant strains were about equally infected up to the sporozoite stage.

The effect of exposure to DDT, if any, on the development of sporogony cycle was not reflected in resistant or in non resistant strains of *C fatigans* as measured by the results of comparative infections. Sporogony cycle was completed in a normal manner in resistant *C fatigans* in which the mechanism responsible for aborting or counteracting the lethal action of the toxicant was activated by one sublethal and three lethal exposures to DDT on alternate days which covered the entire incubation period or by four lethal exposures once daily during the early stages of the parasite development. Likewise the results were similar in non resistant *C fatigans* after exposure to sublethal doses of DDT.

There was no modification of the host parasite relationship when resistant *C fatigans* were subjected to a lethal contact with DDT for as long as six hours.

preceding infective blood feed The presence of absorbed D D T in the surviving specimens did not seem to operate against the conjugating gametes or ookinetes that were being then formed in the stomach of the mosquitoes In other words acquisition of infection was not inhibited

TABLE I

Infection with P relictum in D D T resistant and non resistant strains of C fatigans exposed to D D T

Experiment number	Exposed or not	<i>C fatigans</i>									
		RESISTANT STRAIN					NON RESISTANT STRAIN				
		Number dissected	Gut positive	Glands positive	Total positive	Per cent total positive	Number dissected	Gut positive	Glands positive	Total positive	Per cent total positive
1	Exposed	13	—	7	7	54	2	—	1	1	50
	Unexposed (comparison)	11	—	6	6	55	7	1	3	4	57
2	Exposed	21	—	8	8	38	11	—	5	5	45
	Unexposed (comparison)	21	2	9	9	43	14	—	6	6	43
3	Exposed	51	5	25	30	59	—	—	—	—	—
	Unexposed (comparison)	33	1	18	19	58	—	—	—	—	—
4	Exposed	14	3	5	6	43	—	—	—	—	—

Details —

Experiment 1 Two exposures of 40 minutes each, the first within 12 hours and the second on third day of the infective blood meal in both

Experiment 2 First exposure of 40 minutes immediately after infective blood meal followed by three separate exposures once every other day, of one hour each for resistant *C fatigans* and of 20 minutes each for non resistant *C fatigans*

Experiment 3 Four exposures of one hour each once daily, commencing from the first day of infective blood meal

Experiment 4 A single prolonged exposure of six hours preceding infective blood meal

Note 1 Resistant *C fatigans* were of Generation 43 in Experiment 1 and of Generation 44 in Experiments 2 to 4

2 Dosage of D D T was 200 mg in acetone per sq ft in all exposures

3 Usually only salivary glands were dissected for sporozoite infection In a few cases guts were also examined, particularly if glands were found negative

respectively

DEVELOPMENT OF SPOROLOGY CYCLE OF HUMAN MALARIA IN RESISTANT AND NON-RESISTANT STRAINS OF *A FLUVIATILIS*

Experiment 1—Resistant and non resistant *A fluvialis* were caged separately in screened bamboo rings and applied to a gametocyte carrier of *P vivax*. All the mosquitoes could not be fed on the donor who on account of tender age (three years) would not tolerate mosquito bites. The blood fed mosquitoes being small in number, were not exposed to D D T.

Experiment 2—One lot of resistant and another of non resistant strain were fed simultaneously on a crescent carrier*. Here again, the mosquitoes were not exposed to D D T, in the hope of utilizing them for a neuro-syphilis case under the treatment of the Medical Officer, Government Hospital, Mettupalayam, South India. This, however, did not materialize. The results of dissection of both the experiments are shown in Table II.

TABLE II

Infections with human malaria in D D T-resistant strains of *A fluvialis*

Experiment number	Species of Plasmodium	<i>A fluvialis</i>									
		Resistant strain					Non resistant strain				
		Number dissected	Gut positive	Glands positive	Total positive	Per cent total positive	Number dissected	Gut positive	Glands positive	Total positive	Per cent total positive
1	<i>P vivax</i>	49	2	2	3	6					
		*20	0	0	0	0	*14	0	0	0	0
2	<i>P falciparum</i>	50	4	18	21	40	50	39	39	52	

Note 1 In both the experiments mosquitoes were not exposed to D D T

*2 Partially fed

It would appear that both the resistant and non-resistant strains of *A fluvialis* were almost equally susceptible to infection with human malaria.

DEVELOPMENT OF SPOROLOGY CYCLE OF *P. GALLINACEUM* IN NON-RESISTANT STRAIN OF *A. EGIPTI* AFTER EXPOSURE TO D D T

Experiment 1—In this experiment, mosquitoes were divided into three groups. Females in group (a) were first fed on an infected fowl and then exposed to 25 mg of D D T for five minutes. Out of 300 engorged females, 227 (or 76 per cent)

* Thanks are due to Dr. A. Kanagaraj, Medical Officer, Government Hospital, Mettupalayam, South India, for allowing permission to feed mosquitoes on this patient.

Effect of Exposure to DDT on Sporogony Cycle

were found to have died the following day. In group (b) females were first exposed to DDT as in group (a) and then given a chance to feed on the same infected fowl. Very large numbers of mosquitoes were used because only a small proportion of the excited females could pierce the skin and take a blood meal. The third group (c) which was not exposed to DDT was kept for comparison.

Experiment 2—In this experiment, *Aedes aegypti* females were exposed to DDT (25 mg per sq ft) as gravids for three minutes. The following morning mortality among these mosquitoes was found to be 83 per cent (166 out of 200 females).

The results of dissection of mosquitoes of the different groups of Experiments 1 and 2 are detailed separately in Table III.

TABLE III

Infection with *P. gallinaceum* in non resistant strain of *Aedes aegypti* exposed to sublethal doses of DDT (25 mg per sq ft) for five minutes

Experiment Number	Conditions of experiment	Number dissected	Gut positive	Glands positive	Total Positive	Per cent total positive
1a	First given infective blood meal and then exposed to DDT	36	—	19	19	53
b	First exposed to DDT and then given infective blood meal	19	—	10	10	53
c	Comparison (unexposed)	21	—	10	11	52
*2a	Exposed to DDT as gravids	24	19	14	19	79
b	Comparison (unexposed)	26	16	10	16	61

*Period of exposure only three minutes

It will be seen that a sublethal exposure to DDT of *Aedes aegypti* preceding or succeeding infective blood meal or in a stage of gravidity was found to have no effect on the development of *P. gallinaceum* inside the mosquito host. The index of infection was practically the same in all the groups of *Aedes aegypti* whether exposed to DDT or not.

Experiment 3—This experiment was started with *Aedes aegypti* most of which had recently become infected with sporozoites of *P. gallinaceum* in the salivary glands. About 75 of these females were exposed to 25 mg of DDT per sq ft. for five minutes.

As soon as the exposure was over, the mosquitoes were given an opportunity to feed on a normal fowl (G 79) enclosed suitably inside the cage. The mosquitoes, with developing symptoms of DDT poisoning, were unable to penetrate the skin for a blood feed until after an hour when one female had become engorged. This was dissected immediately and it showed a moderate sporozoite infection of the salivary glands. Again, one hour later, the same fowl was bitten by three

mosquitoes in the course of 25 minutes, of which two were found infective. At this point feeding was discontinued. The normal fowl (G 79) was thus inoculated with sporozoites by bites of three known infective specimens which succeeded to obtain a blood meal after exposure to DDT.

Another group of infected mosquitoes from the same stock was exposed to DDT. A new normal fowl quitoes by holding it bitten by two proved infective mosquitoes one after 50 minutes and another after one hour of the exposure.

Both the normal fowls (G 79 and G 80), which were inoculated with sporozoites by bite of the infective mosquitoes after sublethal exposure to DDT, developed patent infection which ended fatally in one and in a spontaneous recovery of another. The results demonstrate that a sublethal contact with DDT of infective mosquitoes did not render the sporozoites non infective to normal mosquitoes.

The marked change in the biting potential of *Aedes aegypti* after exposure to DDT is noteworthy. The same specimens of *Aedes aegypti* which would have immediately crowded and fed on the fowl in a few minutes were practically unable to do so after exposure to DDT.

Experiment 4—Mulligan *et al* (1940) have reported that sporozoite agglutination in high dilutions of malarial serum is a specific reaction. This test was made use of to find out if sporozoites in salivary glands of *Aedes aegypti* had undergone any change after exposure to 25 mg of DDT for ten minutes. Sporozoites from heavily infected specimens with self amputated legs and almost at death point, were dissected in different dilutions of homologous chronic serum. The results suggest that sporozoites in highly paralyzed *Aedes aegypti* were not impaired antigenically.

Inoculation of sporozoites from a highly paralyzed specimen into a normal fowl (G 81) caused patent infection after an incubation period of eight days, showing thereby that the sporozoites were infective. The parasites reached their peak on the fourth day and disappeared from peripheral circulation on the seventh day.

VIABILITY OF *P. GALLINACEUM* IN INFECTED FOWLS POISONED WITH ORAL ADMINISTRATION OF DDT

Having demonstrated that the development of malaria parasites in resistant and non-resistant fowls, who estimated biologically the effects of BHC and DDT in the bovine blood by feeding arthropods on treated animals. The two experiments carried out are described below.

Experiment 1—One normal fowl was inoculated with the blood of a fowl harbouring chronic infection. When infection first became patent, the fowl was given DDT in olive oil by mouth at the rate of 100 mg per kilogramme of the body weight for three days in succession. On the fourth day, the fowl began to develop early symptoms of DDT poisoning and its blood picture revealed a number of male and female gametocytes. On the same night when the fowl was in convulsions and prostration, it was placed bodily inside a cage containing large numbers of *Aedes aegypti* which became engorged in a short space of time. Soon after blood feed, most of the mosquitoes began to show toxic symptoms. In some specimens, the symptoms deepened and they fell down in the cage. After about 24 hours, more than half the females were dead. A few females which survived to complete the extrinsic incubation period, were dissected for finding out oocysts and sporozoite infection. All the 12 specimens were found infected with both oocysts and sporozoites. These sporozoites were normal in appearance in fresh and stained preparations. One normal fowl which was bitten by two infective specimens developed infection on the ninth day and died of malaria seven days later.

It would appear from the foregoing that in a normal fowl poisoned with DDT, the parasites multiplied and produced viable gametocytes which on being ingested by mosquitoes resulted in the production of sporozoites which in turn were proved to be infective to a normal fowl.

Experiment 2—A normal fowl was inoculated with blood from the fowl with chronic infection. Before infection became patent, the fowl was given DDT in olive oil as in the above experiment on three consecutive days. For some unknown reason, but died on the peripl. the density of gametocytes was adequate the fowl was exposed to the bites of *Aedes aegypti*. The engorged females were slow in developing symptoms of DDT poisoning. After about four hours most of the mosquitoes were unquestionably irritated in varying degrees. The surviving females showed 85 per cent infection of salivary glands with sporozoites (17 out of 20 dissected).

DISCUSSION

It is well known that certain species of mosquitoes have developed resistance to DDT, particularly in areas where DDT has been used extensively and intensively in massive doses. This insecticide resistance may be slight so that mosquitoes are still killed by the insecticide or may have reached a stage where DDT is of little or no practical value in mosquito control. The importance of the development of resistance, particularly in a vector species, would seem to depend largely on whether the ability of a resistant strain to withstand the doses of DDT which would kill a non resistant strain of the same species, would also operate adversely on malaria parasites in an infected mosquito. In discussing the possible effects of residual insecticides on the interruption of malaria transmission Gabaldon (1953) observes 'If physiological resistance appears, its importance may depend on the fact that the sorbed insecticide may injure or not

the malaria parasite in any of its stages in the mosquito a fact unknown at the present time. The same author again records 'Nobody knows what happens to oocysts or to sporozoites inside slightly intoxicated mosquitoes

On the basis of data on hand it is evident that mere acquisition of D D T resistance which was high in *C fatigans* and low in *A fluviatilis* did not result in any concomitant change of the vectorial capacity of these two species. Resistant and non resistant *C fatigans* which originated from the same parent were almost equally infected with *P relictum*. Similarly resistant and non resistant strains of *A fluviatilis* showed no difference in their susceptibility to infection with human malaria.

It is also evident that activation of the mechanism of resistance in resistant *C fatigans* by lethal contact and in non resistant *C fatigans* by sublethal contact with D D T produced little or no effect on the development of sporogony cycle. Both the groups were infected with *P relictum* to about the same extent as were the comparison groups.

It will be further observed that sporogony cycle was completed in a normal manner in resistant *C fatigans* which were exposed to lethal doses preceding infective blood meal or thereafter during the early or entire extrinsic incubation period.

Experiments with *P gallinaceum* indicate that a sublethal exposure to D D T had no effect on the parasite in any stage in *Edes aegypti* and that when D D T was fed orally to fowls the parasites multiplied and gametocytes remained viable.

Finally it would also appear that if contact with D D T resulted in any change physical or chemical in the body of an infected mosquito the malaria parasites were not apparently influenced by it in their natural environments.

It is not known whether D D T absorbed by mosquitoes found its way to the

SUMMARY AND CONCLUSIONS

1. The acquisition of D D T resistance by *C fatigans per se* had no apparent effect on its vectorial efficiency. Both the resistant and non resistant strains originating from the same female were about equally infected with *P relictum* up to the sporozoite stage. There was no change in the host parasite relationship when the mechanism of resistance was stimulated by exposing the resistant strain to lethal doses of D D T preceding infective blood meal or thereafter during the early or entire extrinsic incubation period. Sporogony cycle was completed in a normal manner in resistant and non resistant strains irrespective of the exposure to D D T.

2. Resistant and non resistant strains of *A fluviatilis* were almost equally susceptible to infection with human malaria. Resistance in *A fluviatilis* was of course low but it was clear cut.

POLICY IN RELATION TO MALARIA CONTROL

BY

S R CHRISTOPHERS

(August 1 1955)

How important is policy in measures directed to the control of malaria in a country? By policy is meant all that goes to the thinking out of what should be done. It includes what it is desired to do, what it is possible to do and how this last can best be done. It is sometimes not very clearly thought out, often based on imperfect information and with the best intentions it may not be the best that could be adopted. One thing it very commonly lacks is adequate provision to show what results have been achieved. It is therefore worthwhile to give careful thought to what it is hoped to do, how it can best be done and how if it is done it can really be known to be done.

What it is hoped to do may be the elimination of malaria as a human disease. To have any relation to reality such hope must be more specific in time and place. There are two words in use in the fight against malaria, viz. control and eradication. Those whose expectations are aimed high prefer eradication; those less optimistic use the word control. As in many human affairs a great deal depends on the particular circumstances and what is reasonable to hope in some circumstances would be unreasonable in others. Whatever the objective, however, whether control or eradication, much the same techniques must be used. Malaria is almost unique as a disease in the great varieties of ways in which it may be attacked and the number of techniques that can be used in doing so. The important point that policy has to decide upon is which of these techniques to use. It may be useful to indicate briefly what these techniques are.

Early control measures, following upon Ross's discovery of the mosquito transmission of malaria, were almost entirely based on action taken against the breeding places of *Anopheles*. The only important rivals to such measures were communal quinine prophylaxis and screening. Discovery of Paris Green as a more efficient and easily handled larvicide and the work of Malcolm Watson in Malaya exploiting the use of drainage and other methods of larval control, together with the conception of species sanitation, appeared to show that control through antilarval action was possible and that where it could be carried out it was the method of choice as being the most fundamental. Other measures such as the

trapping and spraying or fumigation of adults, use of communal quinine and protection took their place as measures to be used where antilarval work was unsuitable or as supplementary measures of securing success. So successful in of merely reducing *Anopheles* eradicating once and for all s method were that the area must not be too great, though it was not necessarily restricted to an island, and considerable areas were treated on this basis.

Some operations of this kind have been highly successful e.g., *Anopheles gambiae* which appeared to have invaded Brazil from Africa and there had occasioned serious epidemics of malaria, as a result of a determined and systematic attack launched by the Rockefeller Foundation in association with the Brazil Government under Doctors Soper and Bruce Wilson was completely eradicated from North East Brazil and up to the present (Russell, 1955) Brazil has remained free from this species. Another successful anti *gambiae* eradication operation has been carried out in Upper Egypt (invaded area 4,270 sq miles and population some three million). In Sardinia, at a total cost of 12 million dollars and with the assistance of some thousands of scouts, an attempt was made to eradicate the vector species. But though malaria was eradicated the operations were not completely successful in eliminating the indigenous species of *Anopheles*. In Cyprus, an island with endemic malaria (spleen rate about 25 per cent), there was an example of the use of the new insecticide D D T as a larvicide. Here also an attempt to eliminate the indigenous *Anopheles* was unsuccessful, though as a result malaria was much reduced.

In the first world war antilarval control, with in addition quinine prophylaxis where larval control was impractical or required supplementing, was still the recognized m and other are. Nevertheless in the second world war

In the period between the two wars, two things revolutionized ideas regarding control. These were the discovery of new more and more effective synthetic antimalarial drugs and the results from the new insecticide D D T used in residual spraying. Drug prophylaxis through mepacrine, now as a result of the previous war pushed as a prophylactic measure with the full and effective support of the military commands was practically the answer to malaria control in troops. The new and powerful insecticide D D T, used first as a larvicide and eventually along with a number of related compounds in residual spraying has been so dramatically successful that many have considered it the final answer as to how malaria can be fought.

With this brief resume of the present position with respect to various forms of techniques used against malaria we may usefully examine some considerations that affect policy. It will be most convenient to do so chiefly in relation to experience in India.

AREA AND POPULATION

In Table I, are given the area, population and persons per square mile in a number of tropical malarious countries.

PLATE VIII



II Lt. Col. R. S. RICKARD CHRISTOFFERSEN A. J. D. P. R. M. R. I.
In charge Central Malala Bureau, Kaul 131, 1316 and 1317-1318

TABLE I *

Area, population and persons per square mile in a number of tropical malarious countries

Country	Area in square miles	Population	Persons per square mile
An English county (Cambridge)	49*	177,000	360
Trinidad	1,861	678,000	365
Cyprus	3,570	505,000	140
Sardinia	9,300	1,250,000	131
British Guiana	83,000	450,000	5
Venezuela	352,000	3,325,000	10
" (treated area)	69,000	2,431,000	35
Bolivia	415,000	3,788,000	9
Gold Coast	24,000	2,223,000	92
Nigeria	373,000	31,500,000	83
Belgian Congo	910,000	12,115,000	13
Tropical Africa as a whole (From 10° N to the level of Beira)†	6,000,000	60,000,000	10
Pakistan	304,700	75,840,000	247
India	1,143,000	356,179,000	312

* Data, except for tropical Africa as a whole, from Whittaker's Almanac, 1955

† Area for tropical Africa has been measured from map and given approximately. The figure for population is probably an under estimate.

Such a list serves to show the relative scale of operations that would be required for these countries and emphasizes the special cases of India and some tropical African countries.

ECONOMIC STATUS

There will almost certainly be a great difference in what a prosperous and perhaps largely Europeanised country can do as compared with a relatively poor country much of the population of which may be living in rural or even jungle conditions. Between two such, the whole question of malaria control differs enormously and, except as experiment for some particular purpose, what one might almost term smash and grab operations are not usually the most suitable in the latter circumstances.

VITAL STATISTICS

One point that it is very necessary to know in a country where the question of action against malaria arises is how much malaria there actually is. Normally it is assumed that this will be shown by the vital statistics, as also whether any steps that have been taken have produced the desired result. Unfortunately, where the

thing and cannot be expected to be accurate. In general, vital statistics are of little use except in very special cases in determination of malarial incidence. Hospital records in such countries often represent only a fraction of the real number of cases of a disease. Medical men may be, and usually are, so small in proportion to the population in rural and jungly areas that any attempt to arrive at an estimate of the effect of operations on a large scale through medical diagnosis would be liable to grave doubt. To do so from films sent in to headquarters might be extremely misleading. Unless a good system of returns of death is in existence or there is a sufficiency of effective dispensaries any real estimate of the amount of malaria would require expert investigation.

DISTRIBUTION OF MALARIA

It is not usually that a country is uniformly malarious or even that there are not extensive areas where malaria is not a serious problem. In India there are some considerable areas that come under the designation of healthy. In such areas malaria is often restricted to small foci of infection where conditions happen to be favourable to the disease. Other tracts may be hyperendemic, i.e., malaria is no longer an occasional disease, but one in which infection in childhood is universal, or almost so, and adults are largely immune. Even the children, though infected, often show little evidence of being as seen in some primitive tribes it may be difficult child mortality. On these accounts the urgency action under such conditions has been considered by some authorities to be doubtful. It is a matter of opinion with little factual evidence to go on. Such areas may be quite extensive and have been mapped and much studied in India. In other forms of high incidence communities may be in a miserable state of perpetual illness from malaria and in need of urgent relief. These may be the conditions in communities colonizing new areas and perhaps labour connected with important industries or projects. Without some system of ascertaining what areas and

EPIDEMIC MALARIA

One form of malaria, that termed seasonal epidemic, or when very severe fulminant malaria is especially important. Its characters are sudden onset with

Policy in Relation to Malaria Control

thirty years or more there has been developed a centre of malaria research and control on a scale and with an output of results that can safely be said to be second to none other in the world, viz., that now named the Malaria Institute of India

Only very brief mention can here be given of the history and work of this Institution. A very instructive and complete account, however, will be found given by Covell in two communications, the first dated 1938 in Vol 1 of the *Journal of the Malaria Institute of India* giving the history and work of the Malana Survey of India (1927-1937) and the second dated 1947 in Vol I of the *Indian Journal of Malariology* giving the history and work of the Malaria Institute of India up to that date. Up to 1909, there was in India no organized plan for malaria research or control. In that year, however, proposals were made for a malaria organization for India by Lieut.-Colonel J. T. W. Leslie, Sanitary Commissioner with the Government of India, whose far sighted policy was also responsible for the building up of the Bacteriological Department of the Government of India in which was combined the running of the large Central and Provincial Laboratories and much else. The scheme included a General Committee (with the Minister as President) with a delegate from each Province and Provincial Committees to obtain information and supervise local enquiries. A part of the scheme was the Central Malaria Bureau (1910-1916 and 1919-1927) At the Bureau were instituted a reference library on malaria, collections which later formed the basis for work on the mosquitoes of India, and other activities aimed at advancement of malaria work throughout India and Burma. The Bureau maintained close connection with researches and surveys carried out by the Provincial Malaria Officers many of whose names have been then and later familiar in the literature. It also held an annual class of instruction for medical officers taking up malaria work in which both field work and necessary laboratory techniques were undertaken. Unfortunately the first world war necessitated the calling up of most of the Provincial Malaria Officers for duty in different theatres of war and the organization was for a time in abeyance. Proposals, however, in 1924 for a renewed organization led in 1927 to the formation under the Indian Research Fund of the Malana Survey of India with Lieut.-Col (now Brigadier) J. A. Sinton as Director. At first located at Amritsar, a city severely affected by the 1908 epidemic, it was later moved to Karnal where operations were in progress, but later at the director's suggestion to the present headquarters in Delhi. In 1938, at a meeting of the Indian Research Workers Association, the Government of India agreed to finance the now greatly enlarged organization, which under the name of the Malaria Institute of India continued work under the directorship of Col (now Major General Sir Gordon) Covell, followed on his retirement in 1947 by Lieut.-Col. Jaswant Singh. Throughout these years innumerable surveys have been made of different areas in India, control measures carried out and in almost every field of malaria control practical measures and techniques perfected. Some idea of the extent and variety of the work carried out may be gathered from the list of papers published in the *Journal of the Institute*. In recent years a great deal of study and experimentation has been given to residual spraying and its effects on which many papers will be found in the *Journal*. Should residual spraying be found to give all that it promises one may safely leave its full exploitation in control of malaria to the present director and his expert staff. That there

is no lack of initiative is shown by the recent formation of an associated Society with its own Bulletin, viz, the National Society of India for Malaria and other Mosquito Borne Diseases of which Lieut Col Jawsant Singh is the President and the objects of which include work on filariasis in India which causes much sickness and is a mosquito borne disease

Quite recently I have seen the announcement that a Malaria Institute has been established under the directorship of Dr D Bagster Wilson in tropical East Africa the East African Malaria Unit of the East Africa High Commission having become the East African Institute of Malaria and Vector Borne Diseases Such a step has very much to recommend it

DEVELOPMENTS IN MALARIA CONTROL METHODS DURING THE PAST FORTY YEARS

BY

SIR GORDON COVELL M.D. D.P.H.

(Jul 4 1956)

A PERIOD of 40 years has been selected for this review because it corresponds approximately with the writer's own experience of malaria and its control. The developments which have evolved during this time in the methods used to combat the disease may be considered under the headings of (a) antimosquito measures and (b) chemotherapy.

ANTIMOSQUITO MEASURES

During the first half of the period the measures adopted were directed almost exclusively towards the destruction of the aquatic stages of the mosquito: the egg, larva and pupa, usually referred to as antilarval measures. Some of the earlier campaigns, such as those undertaken in Malaya, Sumatra, Cuba and the Panama Canal Zone, were very successful. They were costly but in each case important financial considerations were at stake and the expenditure was amply repaid by the improvement in health which resulted, particularly among the labour forces employed.

In India the prosecution of antilarval measures received a serious setback from the comparative failure of the campaign undertaken at Mun Mir, later known as the "Mun Mir Drainage Project". The project was largely carried out from outside the protected area. The campaign was further discredited when the great regional malaria epidemic of 1908, one of the most severe ever experienced, swept over the Punjab. Mun Mir lay within the epidemic area and many cases occurred among the troops stationed in the cantonment and their families.

During the next 25 years antilarval measures were practised with some success in various urban areas, in tea, coffee and rubber plantations and in connection with large scale engineering projects. Following Bentley's survey of 1909-1911 a Special Malaria Department was created for Bombay City and a

number of antilarval measures were put in force, directed chiefly towards the prevention of mosquito breeding in wells and cisterns, the favourite breeding places in Bombay of the vector, *A. stephensi*. As a result, the malaria rate was greatly diminished, so much so that the local authorities decided that the measures could be relaxed. Accordingly in 1918 the Malaria Department was disbanded, but the meagre staff remaining proved entirely inadequate to cope with the situation. Covers and trap doors of wells and cisterns were removed or allowed to get into disrepair and numbers of wells which had been sealed were re-opened. The incidence of malaria began to increase and in 1922 the heads of 40 commercial houses sent in a petition to the Corporation drawing attention to the prevalence of the disease in the city and to its harmful effects on commerce. In 1923, the Malaria Department was reconstituted, but much of the work previously accomplished had to be re-done. In 1924, the disease was again very prevalent in Bombay and there were a number of cases among the crews of ships berthed in the docks. A Central Malaria Committee was appointed and the staff increased, but malaria continued to be a serious problem and it was decided to hold another survey of the whole island. This survey, which lasted six months and involved the examination of more than 30,000 children, was carried out by the writer in 1928. The recommendations then put forward, which were directed solely towards the prevention of mosquito breeding, were implemented with excellent results.

In Assam, antilarval work was carried out in a number of tea estates under the auspices of the Ross Institute, notably by Ramsay in and around Labac. An interesting development here was the growing of dense vegetation over ditches, streams and swamps to prevent mosquito breeding. This measure was very successful for some years, but in the course of time the bushes used for shading began to invade the tea, necessitating the employment of extra staff to keep it cut back. Eventually in many instances estates reverted to open drains and oiling for the control of mosquito breeding. A similar course of events occurred in Malaya, where extensive subsoil draining was installed in rubber estates. Here again the measure was at first successful, but eventually the roots of trees grew down in between the tiles in search of water and choked the channels, so that an open space $1\frac{1}{2}$ times the height of the trees had to be left on each side of the pipes. Since a rubber tree may grow to a height of 60 feet or more, a large proportion of the plantation was thus put out of action. In many estates the subsoil pipes were pulled up and substituted by open drains and oiling.

Mention may be made of two engineering projects in India whose construction was made possible solely by the Sarda Canal Headworks Provinces, and the building of Nagpur Railway. The construction of the latter project was held up for 40 years owing to the prevalence of intense malaria, the incidence of the disease among the survey parties being so high that the first three were unable to complete their task, while the fourth succeeded only when every engineering post in the party was duplicated. The construction of the railway was finally made possible by the work of the late Major Senior White, Malariologist to the railway, who instituted rigid antilarval measures in and around the camps in which the labourers were concentrated.

During this period, the chief methods employed for the control of mosquito breeding were drainage and the application of various kinds of oil to water collections. A notable advance was the introduction as a larvicide of paris green, following the demonstration of its value in the field by Barbar and Hayne in 1921. From this period until the advent of D D T paris green was used very extensively in large scale antimalaria campaigns throughout the world. It was the principal method employed in the Brazilian campaign of 1939-40 which resulted in the eradication of *A. gambiae* from that country.

The experience gained during the earlier antimalaria campaign in India and elsewhere showed that the disease could probably be controlled anywhere by antilarval measures, *provided that sufficient funds were available for the purpose*. Under urban and industrial conditions where the population at risk was concentrated in a limited area and where its potential output was economically productive, it could usually be demonstrated that the cost of malaria to the community was considerably greater than that of effective control even by the measures then available. It was the control of rural malaria that for so many years proved an insoluble problem to the health authorities of tropical and subtropical countries. Here the population instead of being concentrated in compact areas is scattered in isolated groups of houses and harbours innumerable. It was indeed controlled in rural areas in certain instances as a demonstration project but only at a cost far greater than any sum which the local authorities could afford. Under such circumstances the only way of ameliorating the condition was to provide treatment for the sick a palliative rather than a control measure.

This was the position as late as 1936 when the publication of the remarkable results achieved in South African villages by the spray killing of adult mosquitoes with pyrethrum insecticides at a moderate cost encouraged the hope that here at last was a weapon which might prove practicable for the control of malaria in rural India. Just at that time a comprehensive scheme of malaria control was being put into operation in Delhi urban area which covers about 75 square miles of country. The quarters occupied by certain selected communities of Government employees located in particularly malarious sections of this area were regularly sprayed throughout the malaria season. The results were remarkably good and in one set of quarters the malaria rate was reduced to 1.4 per cent a figure of 45 per cent being recorded in adjacent quarters which were left unsprayed. The method was immediately recommended for use throughout India for personnel such as police, railway, forest or other government employees and labour forces in estates, mills and other industrial enterprises. It was at first thought that its usefulness would be limited to such conditions but in 1937 it was tried as an experimental measure in 1 extended to a number of experimental work on the Unit of the Rockefeller Foundation International Health Division in certain villages in southern India during the period 1938-41. The first large scale routine application of this measure in Indian villages was however carried out in Mysore State.

When the Bombay State Malaria Organization was created in 1942, the spray-killing of adult mosquitoes with pyrethrum insecticide became an important feature of the control programme in Kanara District. Early results in this area were somewhat disappointing, based on a series of patient res- malaria rate. In September 1945, imported into India for military purposes was made available to the Bombay Malaria Organization for field trials. From then onwards the spray killing of mosquitoes with residual insecticides became the main feature of the campaign, which was progressively extended to cover the whole of the malarious parts of the State.

In the same year a large-scale project was launched in Venezuela with the object of eradicating malaria from the entire country by DDT residual spraying and similar campaign was inaugurated in British Guiana. Since then, DDT spraying projects have been carried out in Brazil, Argentina, Bolivia, Peru, Ecuador, Columbia and French and Dutch Guiana. In the United States a joint programme for eradicating malaria was also launched in 1945, with the result that the disease has now practically scale campaigns are in progress in Italy, Greece, Mauritius, Ceylon, Thailand, as well as in India and Pakistan. In all these projects spraying with residual insecticides has been the chief and in many cases the sole, antimalaria measure employed.

It is interesting to recall that the systematic destruction of adult mosquitoes was practised in the Panama Canal Zone as early as 1908, the first to use it being W. R. Procter, a sanitary inspector. It was done by negro labourers armed with chloroform tubes and acetylene lamps. Mosquitoes were also caught in wire gauze traps, placed over the windows. These measures met with considerable success in reducing the malaria rate. The destruction of hibernating adult mosquitoes by hand catching was also practised in Holland from 1920 onwards, and in 1926 pyrethrum sprays were introduced for this purpose. It was this work in Holland, largely inspired by the insistence of S. P. James on the importance of destroying the infected mosquito and thus interrupting transmission, which formed the basis for the successful campaign in South Africa alluded to above.

CHEMOTHERAPY.

During the first decade of the period under review the only drugs available for the prophylaxis and treatment of malaria were the cinchona alkaloids, of which the most commonly used was quinine. It was customary to give the drug over an extended period, beginning with 20 to 30 grains daily for seven to ten days, this was usually followed by a similar dose twice or thrice weekly for several weeks or even months. During the first world war, quinine was given to the troops in Macedonia in enormous after the relapse of 1,350 grains. Another, known as a sterilizing course, was given to

of quinine orally plus 30 grains intramuscularly daily for 12 days, 60 grains orally for two days, and 20 grains orally for the following two weeks, a total of 1,180 grains

The numerous investigations conducted between the two world wars, notably those sponsored by the League of Nations Malaria Commission together with experience gained during the treatment of neurosyphilis with malaria therapy, resulted in the general adoption of comparatively short courses of treatment for malaria. It was established that any dosage of quinine exceeding 30 grains daily not only fails to affect the course of the disease, but is also detrimental to the health of the patient, and that to extend the course beyond seven days has no effect on the relapse rate.

The evolution of the synthetic remedies now so largely used in the treatment and prophylaxis of malaria makes an interesting story. Quinine is an effective drug for terminating the clinical attack in most malarial infections and it is doubtful if any of the synthetic drugs now in use would have been developed had not the Germans been deprived of all sources of quinine during the first world war. It was the necessity for finding an effective substitute for quinine which inspired the researches which led to the synthesis first of plasmochin (pamaquin) and later of atebnin (mepacrine).

Up to the time when this work was planned, all attempts to synthesize quinine had failed, but Guttman and Ehrlich, many years earlier had discovered that methylene blue stains, and, therefore, presumably penetrates, the malaria parasite and had observed some abatement of clinical symptoms in patients suffering from malar infection to whom the dye had been administered. With these experiments in mind, a team of German scientists embarked on a line of research which was destined to have far reaching consequences. They introduced a basic side chain into the formula of methylene blue, and found that one of the resulting compounds had considerable activity against bird malaria. It seemed likely that the activity of the quinoline . . . the introduction of a similar . . . in the synthesis of pamaquin, . . . effective action against human malaria parasites.

Pamaquin was found to have a powerful destructive action on the gametocytes of *Plasmodium falciparum*, a property not possessed by any of the cinchona alkaloids, another quite unexpected development was the demonstration in India by Sinton and Bird that when used in conjunction with quinine it effected a marked reduction in the relapse rate of malar malaria. In certain respects however, pamaquin proved unsuitable as a therapeutic agent, chiefly by reason of its relatively high toxicity and the fact that it has little action on the asexual erythrocytic forms of *P. falciparum*. The Germans therefore, embarked on further studies, they attached the basic side chain which had been evolved for pamaquin to other heterocyclic nuclei, and finally, in 1930, produced the acridine compound mepacrine.

Mepacrine proved to have a powerful destructive action on the asexual erythrocytic forms of all species of human malaria parasite. It possesses all the antimalarial properties of quinine, and against some strains of *P. falciparum* it is considerably more active. It has, however, the disadvantage of turning the skin yellow and of producing in certain individuals undesirable side-effects.

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of quinine orally plus 30 grains intramuscularly daily for 12 days, 60 grains orally for two days, and 20 grains orally for the following two weeks, a total of 1,180 grains

The numerous investigations conducted between the two world wars, notably those sponsored by the League of Nations Malaria Commission, together with experience gained during the treatment of neurosyphilis with malaria therapy, resulted in the general adoption of comparatively short courses of treatment for malaria. It was established that any dosage of quinine exceeding 30 grains daily not only fails to affect the course of the disease, but is also detrimental to the health of the patient, and that to extend the course beyond seven days has no effect on the relapse rate.

The evolution of the synthetic remedies now so largely used in the treatment and prophylaxis of malaria makes an interesting story. Quinine is an effective drug for terminating the clinical attack in most malarial infections, and it is doubtful if any of the synthetic drugs now in use would have been developed had not the Germans been deprived of all sources of quinine during the first world war. It was the necessity for finding an effective substitute for quinine which inspired the researches which led to the synthesis first of plasmochin (pamaquin) and later of atebnin (mepacrine).

Up to the time when this work was planned, all attempts to synthesize quinine had failed, but Guttman and Ehrlich, many years earlier, had discovered that methylene blue, a synthetic dye, acted as a malarial prophylactic. It was later found that quinine esters, the malaria parasite is in patients suffering from

With these experiments in mind a team of German scientists embarked on a line of research which was destined to lead to the discovery of pamaquin.

against human malaria parasites

Pamaquin was found to have a powerful destructive action on the gametocytes of *Plasmodium falciparum*, a property not possessed by any of the cinchona alkaloids, another quite unexpected development was the demonstration in India by Sinton and Bird that when used in conjunction with quinine it effected a marked reduction in the relapse rate of malarial fever. In certain respects, however, pamaquin proved unsuitable as a therapeutic agent, chiefly by reason of its relatively high toxicity and the fact that it has little action on the asexual erythrocytic forms of *P. falciparum*. The Germans, therefore, embarked on further studies, they attached the basic side chain which had been evolved for pamaquin to other heterocyclic nuclei, and finally, in 1930, produced the acridine compound mepacrine.

Mepacrine proved to have a powerful destructive action on the asexual erythrocytic forms of all species of human malaria parasite. It possesses all the antimalarial properties of quinine, and against some strains of *P. falciparum* it is considerably more active. It has, however, the disadvantage of turning the skin yellow and of producing in certain individuals undesirable side-effects.

After preliminary tests on patients, and later in England, pamaquin and series of field trials under the auspice afforded clear and decisive proof of the high suppressive action of mepacrine in all forms of human malaria, though some uncertainty remained as to the possible harmful effects of long continued administration. When Indonesia fell to the Japanese in 1942, thus cutting off the supply of quinine to the Allies, steps were immediately taken to manufacture mepacrine in large quantities in both Great Britain and in the United States. Mepacrine prophylaxis was rigidly enforced among the Allied troops operating in the South west Pacific and South east Asia Commands. This measure resulted in effective control of malaria in both areas and played an important part in achieving final victory.

The German programme of research on synthetic antimalarials had not ceased with the production of mepacrine. They continued their investigations with the object of producing a drug with the same antimalarial properties but without its disadvantages. Removal of the methoxy-bearing ring from the mepacrine molecule gave rise to resochin (chloroquine), a member of the 4-aminoquinoline group of compounds. Preliminary tests of this drug on a small series of patients in a mental hospital in Germany were interpreted as indicating a considerable degree of toxicity, and further research was undertaken to counteract this supposed defect.

The second world war broke out while this work was still in progress and as field tests of the 4-aminoquinolines were as yet incomplete, the Germans adopted mepacrine as the standard antimalarial drug for their troops. After the occupation of France supplies of chloroquine and of an allied compound, sontoquine, were made available to the French authorities for tests in North Africa, when this area was occupied by the Allies, stocks of these fell into the hands of the Americans, who were already engaged in a gigantic research programme in which more than 14 000 compounds were eventually tested for antimalarial activity.

The Americans found that the early German tests of chloroquine had created an exaggerated picture of its toxicity, they also found it superior to sontoquine as an antimalarial drug. It had the advantage over mepacrine of not causing discoloration of the skin, it was found to be in some respects more active than the latter drug and less likely to produce unpleasant side effects. It was not used to any great extent during the second world war, but was soon afterwards adopted as the standard antimalarial drug for the United States Army. Two other 4-aminoquinolines, amodiaquine (camoquin) and hydroxychloroquine (plaquenil), have similar properties and are claimed to be equally effective.

During the latter half of the second world war, British chemists, adopting a new line of approach produced a biguanide compound, proguanil (paludrine) which proved to have remarkable antimalarial properties. This drug acts on the pre erythrocytic forms of *P. falciparum*, and is therefore, a causal prophylactic of infection due to this species of parasite, it is a good suppressive against all forms of malaria, it inhibits the late sporogonic forms of the parasite, so that mosquitoes feeding on a gametocyte carrier receiving therapeutic doses of the drug do not become infective, it has a lower toxicity than any other antimalarial drug known, and it can be produced at very low cost. Its action on the asexual erythrocytic

forms of the malaria parasite is not sufficiently rapid to render it suitable for treatment of the clinical attack and its principal use is in prophylaxis. Proguanil has been used very extensively for this purpose among troops and civilian populations in Malaya and other parts of the Commonwealth during the post war years with excellent results.

More recently another antimalarial drug of importance has been placed on the market. This is pyrimethamine (Daraprim) a member of the diamino pyridine group. It was synthesized in the United States though many of the

likely to be in prophylaxis. It is active in very small doses and can be produced at relatively low cost.

Proguanil and pyrimethamine share one grave disadvantage namely a tendency to provoke resistance in parasites subjected to prolonged contact with either drug in sub therapeutic dosage. Cross resistance between the two drugs has also been demonstrated. It is not possible to forecast at this stage how far this phenomenon will affect their future use. Fortunately no such tendency has yet been observed in respect of either chloroquine, amodiaquine, hydroxychloroquine, nepacrine or quinine.

Another important new antimalarial drug developed in the United States is primaquine, one of the 8-aminoquinoline series. The researches which led to its production were inspired by the urgent need for preventing relapses of malarial malaria in troops returning from Korea. It is claimed that the maximum tolerated dose of primaquine is twice as high as that of pamaquin and that it is our times as active as the latter drug in the radical cure of malarial malaria. Since its adoption as a routine method of treatment the relapse rate among the United States personnel returning from Korea has fallen to less than one per cent.

COMMENT

No student of malariology can fail to be impressed by the profound influence exerted by the exigencies of war on the development of malaria control measures during the past 40 years.

The greatest advance in the conduct of antimosquito measures during this period was the introduction of DDT. This compound had been synthesized as early as 1874 but its insecticidal properties were not discovered until 1939 when Swiss chemists were searching for a chemical which would destroy clothes moths. DDT was first used on a large scale in the early years of the second world war against the Colorado beetle which threatened the Swiss potato crop at a time when military considerations had made the preservation of all foodstuffs of the utmost importance. The need for a synthetic insecticide has been intensified by the shortage of pyrethrum, the bulk of which was then grown in Dalmatia and Japan and in 1942 DDT was made available to the military authorities in Great Britain and in the United States. It was used with great effect for the prevention of typhus during the Italian campaign and later in the war it was employed on a

large scale by the military authorities for the destruction of mosquitoes and other insect vectors of disease. Although D D T was already in existence when the war broke out, the researches which demonstrated its possibilities as an agent for malaria control were inspired directly by military considerations.

Wartime conditions had an even greater influence on the development of synthetic antimalarial drugs than on that of residual insecticides. As noted above it was the fact that they had been deprived of the sources of quinine during the first world war which inspired the German researches which culminated in the production of pamaquin and mepacrine. Chloroquine was evolved as a further development of the same line of research and its outstanding properties as an antimalarial drug were demonstrated by the Americans in the course of their wartime research programme. The investigations which led to the production of proguanil were begun because the Allies in their turn were cut off from sources of quinine when the Japanese occupied Indonesia. Finally, as already noted primaquine was produced in an attempt to evolve a safe substitute for pamaquin for the treatment of personnel returning from the Korean battlefield.

Thus the wars which have devastated the world during the past 40 years have had at least one beneficial effect, in that they have stimulated the development of synthetic insecticides and drugs which bid fair to rob malaria of most of its terrors and perhaps even to lead to its eventual eradication from the globe.

THE NATIONAL MALARIA CONTROL PROGRAMME OF INDIA

A Review.

BY

B ANANTHASWAMY RAO

(Deputy Director, Malaria Institute of India, Delhi)

(September 12 1955)

INTRODUCTION

AWARENESS of the enormity of the problem of malaria, both from the public health and the socio-economic points of view, has existed in India through several decades. Indeed, it had been repeatedly demonstrated for over two decades in different States that it was feasible to control and prevent malaria efficiently and urban malaria even economically. The social and economic betterment of communities in whom the malaria was controlled, was only too obvious. Between 1946 and 1953, several States had carried out large scale successful antimalaria programmes with indoor residual spray of D D T in the rural areas. At the close of the financial year 1952-1953, about 30 million people out of an estimated 200 million exposed to the risk of malaria, were being protected from the disease at an annual cost of 15 million rupees (Jaswant Singh, 1953).

The need for and the feasibility of a national programme for malaria control had been visualized as early as 1946 when the Health Survey and Development Committee recommended a nation wide effort. It was, however, in 1952 that a plan was formulated as a part of the health development programme of the first Five Year Plan for the country. The Indo-American aid made it possible to launch this first national health drive.

THE PLAN

Extensive knowledge of malaria and methods of its control under widely differing epidemiological conditions involving several vectors, was a great help in the formulation of the Plan. Although based on certain assumptions dependent on the data available, it was dynamic, capable of modifications as and when

necessary. The plan is technically sound and has had necessarily to be an experiment in so far as its administration, organization and execution are concerned.

Programme of India remains to date unique and the biggest in the world. It is proposed to review this programme in retrospect and prospect after three years of execution.

Based on the assumption that 200 million people of the country's population are exposed to the risk of malaria (with an estimated annual morbidity of 75 million and mortality of 0.8 million), the plan was drawn with a defined objective to protect the entire population at risk from further infection. The emphasis of the plan would in retrospect appear to be mainly rural malaria control.

The method of malaria control provided was to intercept the transmission of malaria by the use of insecticides in the dwellings (75 per cent of the population) once or twice and rarely three times a year. The total dosage of 200 mg of technical DDT per person per year. For over all calculation, an average house was reckoned to have one thousand sq ft of indoor surface to be sprayed. Each house was reckoned to have a population of five.

The plan envisaged an operational phase of three years and a maintenance phase thereafter. The financial implication of the plan during the years of the operational phase was estimated at Rs 1505 lakh. The major part of this, namely, Rs 772.7 lakh, was to be American aid in kind (transport, equipment, DDT), while the Government of India was to contribute Rs 227.3 lakh for the expansion of Malaria Institute of India and the provision of antimalaria drugs, locally produced insecticides and customs duty on material coming from abroad. The United Nations International Children Emergency Fund gave Rs 15 lakh worth DDT. The State Governments' contribution was estimated to Rs 490 lakh to cover the salaries of the staff employed and running expenses.

The plan provided for the protection of 125 millions only out of the 200 millions estimated to be at risk. The implementation of the programme was to be phased to set up the required organization in the different States for the protection of 75 millions in the first year of the plan and the full 125 millions during the second and third years. Thereafter, it was expected that the tempo of the control operations would be scaled down to the maintenance phase. It will be seen later that some changes from the original planning had to be made, even within the first three years.

RESPONSIBILITIES

Direction, co-ordination, over all supervision, training of staff, procurement and supply of equipment, transport and insecticides and final assessment were allocated as central responsibilities to be discharged by the Malaria Institute of India. The States were to be responsible for the recruitment of staff, execution of the programme, immediate supervision and concurrent assessment of results.

In accordance with the Constitution, Public Health being a State responsibility, it was necessary to circulate the plan and invite the concurrence of the States to participate in the national effort. Each unit of the National Malaria Control Programme was designed to protect a population of one million and the States were requested to indicate the total number of units required to cover all the malarious areas in each, and the number they could support. It was fully

organization as quickly as possible

IMPLEMENTATION

Saturday, December 13 1952, will be remembered as a landmark in the history of malaria control in India when the relevant operational agreement was signed in New Delhi, between India and the United States of America. That agreement made it possible to equip and provide insecticides transport and equipment for 75 units in 1953-1954, each unit protecting one million population. It was found necessary, however, by a second agreement in the same year to provide for 15 additional units, bringing the total for the first year to 90. Thus addition was made possible by the free grant of 400 tons of DDT by the United Nations International Children Emergency Fund. In March, 1954, as a result for 35 more units, 11 to 136 to protect been increased to

162 by allocating additional 26 units during 1955-1956

It would thus be seen that out of an original estimate of population at risk, namely 200 million, there still remain 38 millions requiring protection

Despite the fact that all details of planning and logistics of supplies, etc., were given due consideration, there were some inevitable birth pains. Perhaps

bottle necks of rail and time for the transport, destinations where they willingness of all concerned

Some Government policy decisions and procedural formalities resulted in the supply of a few items of transport and equipment not suitable for use under the varied field conditions in the country. The trucks, for example, were found to be too large for being manipulated underneath overhead railway bridges, etc. The power sprayers were found to be unusable due to their huge size. These difficulties were freely discussed at a conference of field workers and were got over by local initiative and rectified in subsequent procurement

The insecticide formulation (75 per cent water dispersible powder) received from America was from different manufacturers in that country. In addition, the

periods of storage and transit for various consignments were different from one another. When the first complaint was received about the difficulty of obtaining a good water suspension out of a batch of insecticide received in the country, it became necessary to inspect and test every consignment of insecticide received at the different ports before distributing them to the various States. Simple devices for testing of the insecticide formulations, as well as for rendering them suitable where found to be wanting in the required specifications, were quickly developed with the full cooperation of the U.S. Technical Cooperation Mission to India.

BOTTLE NECKS

There was initial delay in the recruitment of staff both in the Centre and in the States on account of procedural formalities. The latter have also been responsible for long delays in procurement of supplies. It is time that necessary action was taken to see that such bottle necks are not allowed to interfere with the scheduled implementation of an emergency programme like the National Malaria Control Programme.

ACHIEVEMENTS

The training of Malaria Medical Officers and ancillary personnel required, was provided in the plan, and the staff and facilities in the Malaria Institute of India were suitably expanded to meet this obligation. Seventy-five medical officers, six entomologists, 402 malaria inspectors, 14 engineers and 21 laboratory technicians have been trained from 1953 onwards at the Malaria Institute of India. The latter is fully equipped to meet all the future training requirements of the personnel.

To ensure uniformity of methods of control, assessment and accounting it was quickly realized that an operational guide was necessary. This was prepared with due regard to the divergent conditions of endemicity, vectorial behaviour, population density, transmission period, communications and a host of other factors. The document was deliberately called a 'Guide' with the full knowledge that modifications would be necessary from time to time and place to place, to avoid harmful regimentation and provide full scope for individual initiative. A second edition is already in the press.

A detailed assessment of results is being done but the over all picture reveals progress. The results, however, are not, and could not in their nature be expected to be uniform everywhere. The quality and extent of control established with the inauguration of the National Malaria Control Programme has varied from State to State, being more intensive in the State where malaria control operations had been well established prior to the national plan. A few States which had a good nucleus of malaria organization prior to the plan, have, however, not advanced to the degree and extent possible during the plan. One among several reasons for this state of affairs appears to be a conflict in ideology and policies pursued by State Governments with reference to participation on voluntary basis of local people in developmental

plans in general. Such voluntary participation in a malaria control programme has some obvious limitations.

To achieve successful control in the entire country (or even a State) it is essential to spray all the houses in malarious areas for the requisite number of times within as short a period as possible. The time interval between sprayings as well as the spraying periods are governed to a great extent, among other factors, by the periods of the year when malaria transmission actually occurs. Experience has shown that neither of the above conditions can be effectively satisfied by utilizing voluntary labour which is not amenable to any kind of control.

At the time of inception of the plan, there was no agency to manufacture standard spraying equipment in the country and all such equipment had, therefore, to be imported. In pursuance of a general policy local industry was stimulated to interest themselves in the manufacture of this equipment. Full use was made of a specialist in the line, made available to the Institute by The Rockefeller Foundation to draw up a set of standard specifications based on the World Health Organization general specifications for sprayers, to suit local conditions. The industry in the country has in the course of two years been able to produce standard equipment in sufficient number to avoid the necessity of importing this item altogether. Besides, the easy availability of much needed spares has helped considerably in the smooth working of the programme.

The production of insecticides locally during the plan period to make the country as nearly self-sufficient as possible, by mobilizing both public and private sectors in the country, has progressed satisfactorily. One DDT plant established in Delhi as a joint project by UNICEF/WHO/Government of India has gone into production with an annual capacity of 700 tons and a second plant is proposed to be set up in the south with a capacity of 1,400 tons. Steps have already been taken to double the capacity of the Delhi plant. The private sector is producing BHC and it is expected that an equivalent of nearly 1,500 tons of DDT would be available.

ANALYSIS OF RESULTS

The data received from the units in the monthly reports for the year 1953-1954 and 1954-1955 are under compilation and analysis. Appendices I, II and III give (1) the population protected and DDT consumed, (2) the malaria indices, and (3) the morbidity figures.

Appendix I is prepared on the basis of the largest number of houses sprayed in any one round of spraying during the transmission period and assuming the number of people per house as five. The recommended dosage of DDT application is 200 mg per square foot in two applications of 100 mg each. On the basis of the assumption that the number of persons per house is five, it is not possible to give a 200 mg dosage during the transmission season each year and/or if the number of persons per house is more or less than five per house as assumed. It would, therefore, be necessary to make allowances for these variations when

particularly for assessment of results and future policy in respect of some of the States not coming up to expected standard

At the time when the N M C P was planned the factor of anopheline vectors developing resistance to insecticides had not assumed the importance it has within the last year or two. Insect resistance to insecticide was certainly known but observations at that time appeared to indicate that the danger of resistance in anophelines was not so imminent as in the case of other insects which had a lower degree of natural susceptibility to insecticides. But recent studies indicate that the danger is real. The time taken by anophelines to develop resistance requires to be determined. It would probably vary from species to species and a number of factors like dosage of insecticide and its deterioration etc will affect it. In the circumstances if malaria is 'controlled' within the time (actually eradicated) usually then and then thus possibly avoid in use. Thus it is

seen that the time factor has assumed considerable importance. Once the resistance phenomenon is allowed to develop, the problem of rural malaria control with insecticides synthesised with chlorine, may become impracticable. It is because of this factor that we have to re-examine our original objectives and targets and modify them where necessary to suit present day concepts.

The Government of India has decided to provide protection from malaria. The scope of the plan is for 750 lakh (75 million) people. In selecting this population out of the 200 million preference was to be given to those living in hyperendemic areas, the potential food growing areas and for those living in community project areas within them. The concept of eradication will involve the inclusion in the programme of all the areas even those of very low endemicity, and the States which have left out areas with spleen rates less than ten per cent in the original planning will have to reconsider their requirements.

As in the past, the base was limited to three years. The experience elsewhere is necessary to extend it by an additional period of two years so as to continue the full control operations for a period of at least five years. The point to consider now would appear to be whether this additional period of two years followed by the necessary maintenance period would be sufficient to achieve malaria eradication? If eradication is to be the goal then ensurance of its achievement everywhere or at least in large contiguous areas, is of paramount importance. This will require a very careful and continuous vigilance during the maintenance period after the end point is reached and will largely depend on the calibre and application of the vigilance staff in the units.

The indices to determine the achievement of eradication* have necessarily to be more sensitive than the ones we adopt at present to assess malaria control. They will in all probability consume infinitely more time and involve greater expenditure in being determined. One important essential factor in this connection will be a thorough search for every new case of malaria. On this will depend the rest of the epidemiological verification investigation and measures to

eradicate the focus. It will require intensive study to evolve quickly a suitable organization for spotting new cases and their microscopical verification.

It has been indicated that each unit of the National Malaria Control Programme was designed to afford protection to one million population. This has been found to be feasible only under certain conditions of population density, communications, etc. There are, however, areas where population is scarce and communications scanty, in which circumstances the units are unable to cover much more than nearly half a million. It may, therefore, be a more accurate overall estimate to place the target at 800,000 per unit on an average.

The main emphasis of the National Malaria Control Programme was on malaria control in the rural areas. With large rural areas under control and the conception of eradication having come in the fore-front, the problem of urban malaria has taken on a new urgency. In the light of experience and repeated demonstration in this country and elsewhere, urban malaria control should, if feasible, be based largely on permanent engineering measures. Such measures are not only more economical than the measures suited to control malaria in the rural areas but also take care of general mosquito nuisance. Where there are other mosquito borne diseases, indeed, the permanent engineering measures are the ones of choice in their prevention, the second choice being given to recurrent anti-larval measures. To the administrators and the public, the National Malaria Control Programme would appear to have come to mean the spraying of DDT as the

SUPERVISION

It has been pointed out that the pace at which control has been established has been greater in some States than in others. It has also been indicated that such progress has not been uniform even in some of the States that had considerable experience and staff for malaria control prior to the advent of the plan. In the States where there was little or no organization to control malaria prior to the plan, perhaps it was to be expected that the above, it would appear necessary now to for greater supervision where necessary. In centres and utilizing the highly trained and experienced personnel, both at the Centre and the States, to staff such centres, seems essential to achieve the objectives in full during the second Five Year Plan.

RESEARCH

It has been said that a unique contribution to science by America lies in making research a career and a normal avocation. The realization that research is not something that is mystic, and should be pursued in exclusive laboratories by only a few who are removed from conditions in the field, does not yet seem to have pervaded this country, at least not widely enough among practical malariologists. The problems to be solved are many, it is the field malariologist that comes across

the problem at first hand It is he that most requires a solution to each problem
scientific lines Many of the problems of
by work in the field and would be

A number of research projects covering the different aspects of the epidemiology and control are in progress The vectors of malaria in some areas like Tripura, Manipur, Vindhya Pradesh, Madhya Bharat, have been incriminated The insecticidal properties of the newer synthetic insecticides and the best material as also the most economical dosages of application, are under continuous study The normal susceptibility to DDT of the different malaria vector species and their present status after different periods of exposure to DDT, are currently under detailed investigation A technique for working with lower pressures in the spraying equipment has been developed

Perhaps the single most important problem of the day is insect resistance to insecticide The study of the problem requires planning, definition of objectives and priorities—a tremendous amount of work It requires no prophet to say that postponement of this phase of activity will be fatal to the cause of malaria control
trained in
ly to tackle
are to be

exploited before it is too late

PUBLICITY

It is a sad reflection that the progress of health activities in the country, not to mention the National Malaria Control Programme in particular, did not receive adequate publicity in the feature articles commemorating eighth year of freedom The reason for this must be sought Is it because that the National Malaria Control Programme is not sufficiently known to the people and the administrators? And yet in other contexts it has been stated times out of number that the National Malaria Control Programme is one of the very few health programmes under the National Plan that has made good progress and one of the very few projects in the entire plan whose benefits have been within the reach of an average householder The results achieved by the National Malaria Control Programme thus far are concrete and not imaginary or theoretical It would appear that the people and the administrators have not yet felt the tremendous activity with regard to prevention of malaria that is in progress in the country on a scale unprecedented anywhere in the world The necessity to get the people and the administrators to feel the progress and take a live interest, seems only obvious Publicity like everything else has to be planned and organized to be effective

PUBLIC PARTICIPATION

It is a sufficiently recognized principle that success in any large undertaking
tivity The more active the public
undertaking This principle has been
at then is the practical feasibility of

public participation in the National Malaria Control Programme? It would appear to lie in the field of active cooperation with the duties of those who are trained employed and paid to carry out certain functions for protecting the public from malaria. Such cooperation can only be obtained by education of the people in the rationale of the activities.

A technique to carry the people all the way with the progress is to organize malaria committees comprising representative members who will from time to time meet to take stock of the situation progress difficulties and obstacles and take steps to overcome them. Such committees formed at all levels like the panchayat

APPENDIX I

Number of houses sprayed population protected and the number protected per lb of D D T

S a e	1953-54				1954-55				
	Number of houses sprayed at least once	D D T consumed (lbs.)	Popu at on protected	Number of people protected per lb of D D T	Number of houses sprayed at least once	D D T consumed (lbs.)	Populat on protected	Numbe of people protected pe lb of D D T	
Ajmer	4 481	38 8°6	21° 405	5 4	67 080	6 610	335 400	5 1	
Bhopal	88 574	21 867 5	44° 870	20 °	183 074	103 065	915 3 0	8 8	
B har	255 210	87 049	1° 76 050	14 6	1 592 587	77 89	96 935	10 °	
Bombay	3° 35 999	1 638 660	16 264 995	9 9	3 486 399	1 676 54°	17 431 995	10 3	
Coorg	39 479	51 4°8	197 395	3 8	38 801	57 015	194 005	3 4	
Delh	Urban	63 354	38 75°	316 770	8 1	105 657	53 3	518 285	9 9
	Rural	56 1°0	73 118	250 600	3 8	0 673	99 071	353 365	3 5
H machal Pradesh	31 417	19 999	157 085	7 8	160 507	79 193	80° 535	5 0	
Kutch	43 3°8	4 341	216 640	8 9	69 387	34 0°	346 935	10 1	
Madhya Bharat	235 738	198 077	1 178 690	6 0	273 446	283 364	1 367 230	4 8	
Madhya Pradesh	1 487 745	451 8°1	7 438 7°5	16 4	1 558 0°2	683 655	7 794 810	11 4	
Man pur	3 461	790	17 305	21 9	86 50	24 950	33 510	13 3	
Mysore	687 43	367 096	3 437 100	9 3	635 6 9	63° 375	3 178 140	5 °	
O issa	310 967	203 895	1 534 835	7 6	1 65° 27	461 313	5 61 300	11 4	
Punjab	214 074	208 34°	1 070 370	5 1	544 34°	610 307	2° 7 1 710	4 5	
P E P S U	159 157	77 958	795 785	10 °	409 956	256 99°	2 049 780	9	
Tr pura	27 4°8	7 398	137 140	18 5	1 0 877	49 923	604 385	1° 1	
Uttar Pradesh	155 584	48 413	777 9°0	16 0	296 7°4	239 703	1 915 855	7 9	
West Bengal	2 718 430	1 118 167	13 59° 150	1° 1	3 181 989	1 481 459	15 909 945	10 7	

APPENDIX II.

Spleen rate, parasite rate and infant parasite rate in different States in India

State	1953-54			1954-55		
	Spleen rate (per cent)	Parasite rate (per cent)	Infant parasite rate (per cent)	Spleen rate (per cent)	Parasite rate (per cent)	Infant parasite rate (per cent)
Andhra	24 4/27 5	3 3/7 2	1 0/7 3	10 0/29 6	7 4/9 7	5 6/7 9
Bihar	11 9/59 6	9 5/16 8		11 2/39 6	0/21 3	0 0/13 3
Bombay	0 0/20 7	0 0/9 7	0 0/8 8	0 0/14 0	0 0/10 0	0 0/13 "
Coorg	0 0/2	0	0	0 0/2	0	0
Delhi	Urban	0 18	0	0 0/6	0	0
	Rural	1 30	0 1	0 80	0	0
Hyderabad	3 9/21 0	0 6/30 6	0	4 0/20	0 6/7 2	0 14
Kutch	6 4	13 4		4 1	5 8	
Madhya Bharat	7 8/26 6	14 7/23 0		14 5/25 6	9 9/15 7	
Madhya Pradesh	8 6/64 9		0/28 7	6 4/44 9	0/32 4	0/17 8
Manipur	23 3	1 5		17 7	1 0	0 8
Mysore	0/12 2	0/15 0	0/5 1	1 2/13 4	0 1/15 9	0/0 3
Orissa	29 9/41 5	1 6/1 9	3 8/33 3	24 7/27 3	0 3/1 7	0
Punjab	7/14 8		0/0 6	3 3/9 0	0/17 3	0/0 8
PEPSU	7 5/7 6	0 2/2 1	0	0 5/2 5	0	0
Saurashtra	22 1	0 6	0	11 1	0 5	0 9
Travancore Cochin	19 2	7 1	0	10 6	1 4	0
Tripura	55 8	17 1	14 2	61 1	21 6	12 5
Uttar Pradesh	5/24 9	0 6/15 5	0/14 2	11 4/28 3	1 5/10 1	0/11 4
Vindhya Pradesh	18 7/27 8			7 9/16 4		
West Bengal	5 3/64 1			2 7/53 0		

Note.—For purposes of conciseness, the spleen parasite and infant parasite rates are presented as ranges in each State. The numerator in each instance represents the lowest rate and the denominator the highest amongst the different units in operation in each State.

public participation in the National Malaria Control Programme? It would appear to lie in the field of active cooperation with the duties of those who are trained employed and paid to carry out certain functions for protecting the public from malaria. Such cooperation can only be obtained by education of the people in the rationale of the activities.

A technique to carry the people all the way with the progress is to organize malaria committees comprising representative members who will from time to time meet to take stock of the situation progress difficulties and obstacles and take steps to overcome them. Such committees formed at all levels like the panchayat municipal district, State regional and national levels would help to keep the plan alive and bring home to the people the full realization of the possibilities of a nation free from such a crippling disease as malaria.

APPENDIX I

Number of houses sprayed population protected and the number protected per lb of DDT

State	1953-54				1954-5				
	Number of houses sprayed at least once	DDT consumed (lbs.)	Population protected	Number of people protected per lb. of DDT	Number of houses sprayed at least once	DDT consumed (lbs.)	Population protected	Number of people protected per lb. of DDT	
Ajmer	4° 481	38 8 6	21° 405	5 4	67 080	62 610	335 400	5 1	
Bhopal	88 74	21 867 5	44° 870	20 °	183 074	103 065	915 370	8 8	
Bihar	255° 210	87 049	1 276 050	14 6	1 592° 587	77 892	7 962° 935	10 2	
Bombay	3 22° 999	1 638 060	16 264 995	9 9	3 486 399	1 676 542	17 431 995	10 3	
Coorg	39 479	51 428	197 395	3 8	38 801	57 012	194 005	3 4	
Delh	Urban	63 354	38 752	316 770	8 1	105 657	23 322	518 282	9 9
	Rural	56 120	73 118	220 600	3 8	70 673	99 071	353 362	3 5
Himachal Pradesh	31 417	19 899	157 085	7 8	160 507	79 133	802 53	5 0	
Kutch	43 3 8	24 341	216 640	8 9	69 387	34 022	346 935	10 1	
Madhya Bharat	235 738	196 077	1 178 090	6 0	273 442	283 364	1 367 230	4 8	
Madhya Pradesh	1 487 45	4 1821	7 438 722	16 4	1 528 9 2	693 655	7 704 810	11 4	
Manipur	3 461	790	17 305	21 9	66 502	219 0	332 510	13 3	
Mysore	687 432	367 096	3 437 160	9 3	632 6 9	622 375	3 178 140	5 2	
Orissa	310 967	203 892	1 534 835	7 6	1 022 272	421 313	222 1 360	11 4	
Punjab	214 074	208 342	1 070 370	5 1	544 342	610 307	2 721 710	4 4	
P. E. P. S. U.	159 157	77 958	795 782	10 2	409 926	226 99	2 049 780	7 9	
Trichura	27 428	7 398	137 140	18 5	1 0 877	499 3	604 382	12 1	
Uttar Pradesh	125 584	48 413	777 9 0	16 0	296 724	239 793	1 915 852	7 9	
West Bengal	2 718 430	1 118 167	13 592 150	12 1	3 181 989	1 481 459	15 909 945	10 7	

APPENDIX II

Spleen rate, parasite rate and infant parasite rate in different States in India

State	1953-54			1954-55		
	Spleen rate (per cent)	Parasite rate (per cent)	Infant parasite rate (per cent)	Spleen rate (per cent)	Parasite rate (per cent)	Infant parasite rate (per cent)
Andhra	21 4/27 0	3 3/7 2	1 0/7 3	19 9/29 6	7 4/9 "	0 6/1 9
Bihar	11 9/59 6	9 5/16 8		11 2/39 6	0/21 7	0 0/11 3
Bombay	0 0/20 7	0 0/9 7	0 0/8 8	0 0/14 9	0 0/10 0	0 0/13
Coorg	0 02	0	0	0 02	0	0
Delhi	Urban	0 18	0	0 06	0	0
	Rural	1 30	0 1	0 40	0	0
Hyderabad	3 9/21 0	0 6/30 6	0	4 0/8 0	0 6 7 2	0/1 4
Kutch	4 4	13 4		4 1	5 8	
Madhya Bharat	7 8/26 8	14 7/23 0		14 5/20 6	9 9/15 7	
Madhya Pradesh	6 6/64 9		0/28 7	6 4/44 9	0/32 4	0/1 8
Manipur	23 2	1 5		17 7	1 0	0 8
Mysore	0/12 2	0/15 0	0/5 1	1 2/13 4	0 5/10 9	0/0 3
Orissa	29 9/41 5	1 6/1 9	3 8/33 3	24 7/27 3	0 3/1 7	0
Punjab	7/14 8		0/0 6	3 3/9 0	0/17 3	0/0 8
P.E.P.S.U.	7 5/7 6	0 2/2 1	0	0 5/2 5	0	0
Saurashtra	22 1	0 6	0	11 1	0 5	0 9
Travancore-Cochin	19 2	7 1	0	10 6	1 4	0
Tripura	55 8	17 1	14 2	61 1	21 6	12 6
Uttar Pradesh	5/24 9	0 6/15 5	0/14 2	11 4/28 3	1 5/10 1	0/11 4
Vindhya Pradesh	19 7/27 8			7 9/16 4		
West Bengal	5 3/64 1			2 7/03 0		

Note—For purposes of comparison, the spleen, parasite and infant parasite rates are presented as ranges in each State. The numerator in each instance represents the lowest rate and the denominator the highest amongst the different units in operation in each State.

public participation in the National Malaria Control Programme? It would appear to lie in the field of active cooperation with the duties of those who are trained employed and paid to carry out certain functions for protecting the public from malaria. Such cooperation can only be obtained by education of the people in the rationale of the activities

to overcome them. Such committees formed at all levels like the panchayat

APPENDIX I

Number of houses sprayed population protected and the number protected per lb of D D T

State	1953-54				1954-55				
	Number of house sprayed at least once	D D T consumed (lbs.)	Population protected	Number of people protected per lb. of D D T	Number of houses sprayed at least once	D D T consumed (lbs.)	Population protected	Number of people protected per lb. of D D T	
Ajmer	4 481	38 826	1 ^a 405	5 4	67 080	6 610	335 400	5 1	
Bhopal	89 574	91 867 5	44 870	90 "	183 074	103 065	915 370	8 8	
Bihar	255 910	87 049	1 766 050	14 6	1 592 587	77 899	7 969 935	10 "	
Bombay	3 30 999	1 632 660	16 964 995	9 9	3 486 399	1 676 549	17 431 095	10 3	
Coorg	39 479	51 498	197 395	3 8	38 801	57 015	194 000	3 4	
Delh	Urban	63 354	39 759	316 770	8 1	105 657	53 32	518 980	9 9
	Rural	56 190	73 118	950 600	3 8	70 673	99 071	353 360	3 5
Himachal Pradesh	31 417	19 899	157 085	7 8	160 07	79 133	809 530	6 0	
Kuch	43 3 8	24 341	916 640	8 9	69 387	34 099	346 935	10 1	
Madhya Bharat	935 738	196 077	1 178 090	6 0	973 446	983 364	1 367 930	4 8	
Madhya Pradesh	1 487 745	4 1891	7 438 7 5	16 4	1 558 999	683 655	7 94 810	11 4	
Manipur	3 461	790	17 300	91 9	66 509	91 950	339 510	13 3	
Mysore	687 439	367 096	3 437 160	9 3	630 6 9	639 375	3 178 140	5 "	
Oissa	310 967	903 890	1 534 835	7 6	1 659 979	461 313	5 961 360	11 4	
Punjab	914 074	908 349	1 070 370	5 1	544 349	610 30	9 791 710	4 4	
P E P S U	159 157	77 938	795 780	10 2	409 956	956 99	9 049 780	7 9	
Trichura	97 498	7 398	137 140	18 5	120 877	49 993	604 385	19 1	
Uttar Pradesh	1 55 584	48 413	777 990	16 0	996 94	939 793	1 010 8 0	7 9	
West Bengal	2 718 430	1 118 167	13 59 150	12 1	3 181 989	1 481 459	15 909 945	10 7	

REFERENCES

HEALTH SURVEY AND DEVELOPMENT COMMITTEE
(1946)

JAIWANT SINGH (1953)

SINTON J A (1939)

Report : Manager of Publications, Delhi
National Malaria Control Programme *Bu' Nat*
Soc Ind Mal Mosq Dis 1, 1 p 9
What malaria costs India? *Health Bulletin* No 26,

WORLD HEALTH ORGANIZATION (1954)

APPENDIX III.

State-wise reduction in malaria cases from the year 1953-54 to 1954-55

State	MALARIA CASES REPORTED FROM HOSPITALS AND DISPENSARIES			On the assumption that one out of 10 cases reported to a dispensary, the total figure of fall in cases arrived at by multiplying the figures in Col 4 by 10
	1953-54	1954-55	Reduction from 1953-54 to 1954-55	
1	2	3	4	5
1 Bhopal	1,44,205	1,00,774	43,430	4,34,300
2 Bihar	11,17,819	7,59,410	3,48,409	34,84,090
3 Bombay	2,53,006	1,95,229	57,777	5,77,770
4 Coorg	3,439	3,210	229	2,290
5 Delhi	9,172	7,035	2,137	21,370
6 Himachal Pradesh	1,01,110	81,838	19,272	1,92,720
7 Hyderabad	1,04,776	56,740	48,036	4,80,360
8 Kutch	18,202	12,094	6,108	61,080
9 Madhya Bharat	1,10,638	90,782	19,856	1,98,560
10 Madhya Pradesh	5,88,716	3,32,678	2,56,038	25,60,380
11 Madras	1,56,099	1,30,454	25,645	2,56,450
12 Manipur	65,260	55,813	9,447	94,470
13 Mysore	1,93,530	1,45,053	48,477	4,84,770
14 Orissa	14,234	7,192	7,042	70,420
15 P F P S U	1,03,330	61,505	41,825	4,18,250
16 Punjab	5,08,636	3,50,496	1,28,140	12,81,400
17 Saurashtra	47,597	33,381	14,216	1,42,160
18 Travancore Cochin	55,012	51,478	3,534	35,340
19 Tripura	1,27,339	90,877	36,462	3,64,620
20 Uttar Pradesh	6,03,644	5,55,882	47,762	4,77,620
21. Vindhya Pradesh	94,314	64,741	29,563	2,95,630
22 West Bengal	16,18,924	8,76,955	7,41,969	74,19,690
Total	67,29,001	40,93,627	19,35,374	1,93,53,740

Notes—The Director of Public Health, Andhra, has reported that 3,507 deaths occurred from malaria in 1954 as compared to 3,526 deaths in 1953.

The Civil Surgeon, Ajmer, has stated that there was about 40 per cent fall in the number of malaria cases from 1953-54 to 1954-55.

National Malaria Control Programme did not operate in the States of Assam, Jammu and Kashmir, Rajasthan and Coalfields during 1953-55.

REFERENCES

HEALTH SURVEY AND DEVELOPMENT COMMITTEE
(1946)

JASWANT SINGH (1953)

SINTON, J. A. (1939)

WORLD HEALTH ORGANIZATION (1954)

Report Manager of Publications, Delhi

National Malaria Control Programme Bu' Nat

Soc Ind Med Mosq Dis, 1, 1, p 9

What malaria costs India? *Health Bulletin* No 26,

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MALARIA CONTROL IN THE PUNJAB (INDIA) WITH SPECIAL REFERENCE TO THE NATIONAL MALARIA CONTROL PROGRAMME

BY

DEV RAJ MEHTA, M SC, PH D (Cantab).

(*Malariaologist, Malaria Organization, Punjab*)

(September 1955)

THE Punjab is a border State at the extreme north west corner of India. After the partition of this Province in 1947, the State has been greatly truncated and instead of 27 districts, it consists at present only of 13 districts. Except for the entire Kangra District and a small portion of Simla which are mountainous, the rest of the State is a great alluvial plain which stretches from the foot of the Himalayas to the Rajputana desert. In other respects the country is featureless with the exception of mighty rivers which traverse the plains and are flooded almost every year after heavy monsoon rainfall. The affected country-side is inundated extensively resulting in the loss of lives, property and outbreaks of malaria and other epidemic diseases.

The soil of the Punjab is for the most part a fine silt deposited by the rivers whose action has virtually formed the land. It is peculiarly impervious to water in most places and this, added to the level character of the country, results in large surface collections of water in the event of floods temporarily submerging extensive tracts of the State.

Between the rivers of the Punjab are strips of country known as the 'Doabs'. These are situated on comparatively high level but they are not entirely safe from being adversely affected by heavy rainfall. On the whole, the soil is very suitable for production of chief agricultural crops namely, cotton, wheat, sugarcane, millets, gram, rice, etc. There is an extensive network of canals throughout the State which greatly help in the production of superior agricultural crops. Other modes of irrigation are by wells in the plains and 'Kuhls' in the hill tracts.

According to the 1951 census, the total population of the Punjab has been estimated at 12,641,205 spread over a land area measuring 37,378 square miles. The distribution of the population in 13 districts of the State is given below —

TABLE I.

Distribution of rural and urban population in the Punjab (India).

District	Total population	Rural population	Urban population
1 Hissar	1,045,645	877,945	167,700
2 Rohtak	1,129,046	970,987	151,059
3 Gurgaon	967,664	827,511	140,153
4 Karnal	1,079,379	876,067	203,312
5 Ambala	943,734	695,784	247,950
6 Simla	46,150		46,150
7 Kangra	936,042	893,592	42,450
8 Hoshiarpur	1,091,986	986,962	105,024
9 Jullundur	1,055,600	761,202	294,398
10 Ludhiana	808,105	602,218	205,887
11 Ferozepore	1,326,520	1,101,438	225,082
12 Amritsar	1,367,040	958,533	408,507
13 Gurdaspur	851,294	688,034	163,260
Total	12,641,205	10,240,273	2,400,932

As is usual in India, the rural population greatly exceeds the urban, being nearly eighty per cent of the total. There are only three cities namely Amritsar, Jullundur and Ludhiana with a population exceeding 100,000. The housing conditions are more or less similar in the rural areas of the State. The villages consist of solid mud built houses, lying compactly around the agricultural lands. In the hill tracts, however, a village is conventional aggregate of small hamlets known as 'Tikas' which are remotely scattered according to the situation of the agricultural land of the villagers. The houses in the hills are usually smaller as compared to those in the plains.

The partition of the Punjab during August 1947 involved considerable exchange of populations between the East and West Punjab—the latter having become part of Pakistan. This exchange had a tremendous influence in introducing East Punjab retain highly as populated predominantly by Muslims, had shown substantial lowering of malarial incidence after this mass exodus of infected Muslim population.

The normal climate of the Punjab is characterized by extremes of cold and hot weather. The cold weather gradually gives way to the hot weather at the end

of March, from which time it gets steadily hotter, and the relative humidity gets steadily less and less till the middle of June when great extremes of heat and dryness are normally experienced. The monsoon breaks suddenly usually about the third week in June, with a consequent increase in the relative humidity and decrease in the maximum temperature. The minimum temperature at night remains practically unchanged at about 80°F. Periodical rain falls throughout the monsoon during July and August, gradually diminishing in September when the relative humidity again decreases. Gradually the winter is ushered about the middle of November. It has been observed (MacDonald and Majid 1951) that the monsoon is the sole apparent climate controlling factor in the spread of malaria, the amount of rainfall influencing the number of breeding places and the associated increase in humidity, which lasts just as long and no longer than the monsoon, making it possible for the anophelines to live a long time and consequently to be capable of transmitting malaria.

INCIDENCE OF MALARIA

Nearly seven million out of a total population of nearly 12.6 million in the Punjab live in rural malarious tracts. This disease is chiefly prevalent in the plains of the Punjab but in the hill tracts at an altitude varying from 200 to 4000 feet above sea level, it has been reported to be very active. Extensive areas in Kangra District are known to be highly malarious and in certain parts conditions of malarial hyperendemicity have also been recorded.

Malaria is endemic almost throughout the Punjab and manifests itself chiefly in the Kangra hill tracts the malaria comparatively more favourable

In the plains of the Punjab, a very large number of endemic tracts exist which although may not exhibit epidemic conditions for years are in some ways so predisposed to them that on a certain minimum of rainfall they will become the seat of epidemic malaria. Such tracts are located mostly near the rivers. In addition, there are other areas which are not obviously riverain but nevertheless behave in the same way. Such tracts usually receive much of the drainage from the district in which they are situated. The foot hills throughout the State, more particularly near the Siwaliks in Hoshiarpur District develop epidemic conditions in this manner. Such tracts not only easily become affected but exhibit a high degree of malarial intensity.

As a measure of the endemicity of malaria the spleen and parasite indices have been studied during the course of malaria surveys conducted in different parts of the State in the recent years.

Before the National Malaria Control Programme was introduced in the Punjab, the spleen rates amongst children under ten years of age in some of the important endemic areas of the State were as under —

District	Locality	Spleen rate (Per cent)
Kangra	Jowali	70 1
	Kulu	33 1
	Jowalamukhi	22 9
	Dera Gopipur	58 0
	Kangra	12 9
	Shahpur	24 3
	Nurpur	43 0
	Indaura	66 6
Gurdaspur	Behrampur	51 1
	Norat Jamal Singh	28 1
	Siri Gobindpur	27 5
	Derababa Nanak	20 0
Amritsar	Patti	70 1
	Ram Das	27 9
	Taran Taran	24 5
	Ajnala	21 6
	Lopoke	29 8
	Majitha	21 6
	Chahal	24 2
	Tung Bala	58 0
	Amritsar	40 5
Ferozepore	Guru Harsahai	89 3
	Zira	49 3
	Dharamkot	22 1
Ludhiana	Sidhwan Bet	47 6
	Machiwara	21 1
Hoshiarpur	Santokh Singh	31 1
	Gagret	14 0
	Amb	25 0
	Garh Shanker	22 9
	Hajipur	26 6

} Suburban area

District	Locality	Spleen rate (per cent)
Karnal	Indra	38.0
	Thanesar	6.9
	Bagda	31
	Khojgpur	34.3
Rohtak	Gohana	3.6
	Juan	3
	Mundiana	3.8
Gurgaon	Dhauj	2.8
	Sohna	7.3
	Punahana	3
	Hasanpur	4
Ambala	Panchkoola	1
	Chamkaur	1.4

It is evident that conditions of high endemicity and hyperendemicity prevailed in the Punjab before the National Malaria Control Programme was reduced in 1953.

Three species of malarial parasite, namely *P. vivax*, *P. falciparum* and *P. malariae* have been detected in the blood films examined from various parts of the State. The last named species is however very much restricted in its distribution.

At intervals of years wide spread epidemics of malaria are liable to occur in this State. The disastrous epidemic of malaria which broke out during 1908 in the Punjab, was of such a type where, in the space of three months it occasioned over 300,000 deaths amongst a population of approximately 20,000,000. Even before this malarial epidemics of marked intensity had been experienced in 1868-69, 1877-78, 1895-96 and in 1899-1900 (Gill 1928). Subsequent to the year 1909 there have been several epidemics of malaria but the outstanding outbreaks were recorded in the years 1917 and 1923, 1947 and 1950. Such epidemics of malaria usually develop during years of excessive monsoon rainfall associated with overflow of rivers following a series of years in which the rainfall has been in defect, and the greater the number of years which have elapsed since the last epidemic year, the more likely is an epidemic to occur.

As a result of the study of distribution of these malaria epidemics during the long series of years it has been found that the districts of the Punjab vary in their liability to experience visitations of epidemic malaria. For instance they do not occur in any part of the Himalayas although Kangra Valley is one of the most intensely malarious tracts. The precise location of such wide spread epidemics of

malaria is more or less restricted to the low-lying plains which are liable to inundation

Amongst the chief factors which complicate malaria problem in the Punjab may be included (1) flooding of the rivers and the associated storm-water channels after excessive monsoon rainfall, (2) canal irrigation, (3) uncontrolled flow of storm water from hill sides into the adjoining low lying plains after heavy rains, (4) extensive swamps in low-lying areas which receive local drainage, as in Gurdaspur District and (5) the impounded water as a result of the construction of protective embankments in certain districts

At least nine districts in the Punjab, namely, Gurdaspur, Amritsar, Ludhiana, Jullundur, Hoshiarpur, Ferozepore, Karnal, Rohtak and Gurgaon are liable to inundations to a greater or lesser extent almost every year following excessive monsoon rainfall when the rivers Ravi, Beas, Sutlej and Yamuna are in spate. Owing to the impervious nature of the soil, the flood water is retained for a sufficiently long period to create malarogenic conditions in such tracts

It is true that malaria has followed canal irrigation in the Punjab by raising the level of subsoil water and created swampy conditions in the adjoining areas. Canal irrigation has become gravely prejudicial to health in areas where it has been improperly carried out. Most of the districts in the Punjab, which are traversed by the great canal system, have become greatly menaced by malaria.

In the hill tracts, the high incidence of malaria is usually associated with paddy cultivation which depends on the water supply from 'Kuhls' arising from hill-streams

MALARIA FORECAST.

The Punjab perhaps claims a unique position inasmuch as it is only in this State that attempts have been made to develop and bring into administrative use a method for forecasting epidemics of malaria. This method, as elaborated by Gill (1928) and Yacob and Satya Swaroop (1944), utilizes information pertaining to rainfall, enlargement of spleen amongst school children, economic conditions, and the variability of malarial incidence in individual localities recorded in previous years.

This forecast, which is issued every year in the beginning of September, has proved of considerable value in past years in indicating areas in which more than ordinary prevalence of malaria has in fact subsequently occurred. A malaria forecast of this type is certainly invaluable to a State which is every year exposed to malaria epidemics owing to the vagaries of monsoon rainfall.

ANOPHELINE FAUNA

There are at least thirteen species of anopheline mosquitoes found in the East Punjab. These are listed below —

A. culicifacies
A. fluviatilis
A. stephensi

A. maculatus
A. annularis
A. pallidus

A. lindesayi
A. pulcherrimus
A. splendidus
A. hyrcanus

A. subpictus
A. barbirostris
A. gigas similis

Of these anophelines, *A. culicifacies* is the accepted chief vector of malaria in the Punjab. This is evident from the following results of dissections, carried out by different workers from time to time —

Observer	Species dissected	Number dissected	Gut infected	Gland infected
Perry (1910)	<i>A. culicifacies</i>	100		
Gill and Singh (1917-20)	—do—	990		
Chowdhury (1930)	—do—	182	15	
Hicks and Majid (1931-36)	—do—	8810	0	3
Mehta (1940-42)	—do—	455	1	6
Gill (1925)	<i>A. stephensi</i>	155	3	1
Chowdhury (1930)	—do—	3		
Hicks and Majid (1931-36)	—do—	204		1
Mehta (1940)	<i>A. stephensi</i>	42		
Chowdhury (1930)	<i>A. fluviatilis</i>	24	2	
Hicks and Majid (1931-36)	—do—	381		1
Mehta (1940)	—do—	140		
Mehta (1940)	<i>A. maculatus</i>	21		
Mehta (1940)	<i>A. pallidus</i>	103		
Chowdhury (1930)	—do—	7		
Chowdhury (1930)	<i>A. splendidus</i>	26		
Hicks and Majid (1931-36)	—do—	98		
Mehta (1940)	—do—	21		
Stephens and Christophers (1902)	<i>A. subpictus</i>	496		
Gill (1917)	—do—	102		
Hicks and Majid (1931-36)	—do—	159		
Hicks and Majid (1931-36)	<i>A. annularis</i>	206		
Mehta (1940)	—do—	190		

From the above data it would be evident that *Anopheles stephensi* and *A. fluviatilis* have also been incriminated in the carriage of malaria. According to

Covell (1927), sporozoites were detected in the salivary glands of *A. culicifacies* James by Adie (1911) in the Kangra Valley. The precise role of this species in the transmission of malaria is being studied.

The dissections of *A. culicifacies* during different months of the year have indicated that the transmission of malaria is active chiefly from August to October. In view of the fact that the transmission is so restricted, the measures aimed at the destruction of anopheline vectors have to be regulated accordingly.

PREVIOUS HISTORY OF ANTIMALARIA WORK IN THE PUNJAB

The first serious attempt to study malaria problem in the Punjab relates to a report of a committee assembled to enquire into the salubrity of the area near Karnal watered by the Western Jamuna Canal (Dempster *et al*, 1847).

In the year 1908, the Punjab was visited by a regional malaria epidemic of marked severity in consequence of which an Imperial Malaria Conference was held at Simla during October 1909 and this led to the creation of the Punjab Malana Bureau. The functions of this institution were confined solely to the study of malaria in this Province. Sometime later Christophers (1911) wrote a comprehensive memoir entitled *Malaria in the Punjab* which embodied a scientific exposition of the intricate malaria problems of the State. These findings laid the foundation for further investigations on malaria (Perry, 1911, and Gill, 1914, 1915, 1917, 1920, 1921, 1923, 1924, 1928).

During the subsequent reorganization of the Public Health Department Punjab, in 1923, the scope of the Malana Bureau was enlarged so as to include the investigation and control of other epidemic and endemic diseases also. This resulted in weakening the efforts towards the study of malaria. In the year 1939 a field epidemiological unit was set up which was responsible for conducting malaria investigations and instituting antimalaria measures which consisted chiefly of the destruction of anophelines by pyrethrum sprays and administration of antimalaria drugs to the sick. In addition limited antilarval measures were also applied.

At the recommendations of the Bhore Committee (1946), a malaria organization was set up for the State with its headquarters at Lahore but before it could establish itself, the Punjab was faced in 1947 with partition based on political considerations.

Prior to the year 1950, antimalaria measures were applied in the Punjab in a very restricted manner by the provision of a small antimalaria unit in each district and consequently feverish endeavours had to be made whenever serious outbreaks of malaria were reported. Such recurring measures proved very expensive and helped in providing relief only for the time being.

In the year 1950, the antimalaria policy was revised under the guidance of Lt-Colonel Jaswant Singh, Director, Malaria Institute of India. Accordingly, the existing State Malaria Organization was expanded with its headquarters at Karnal. Specialized laboratories were set up in various districts and other demonstration

cognate p

units were set up for combating rural malaria in Karnal and Gurgaon Districts and another malaria control project unit was detailed to demonstrate if malaria could be controlled in a badly affected urban tract like the city of Amritsar. During the period from the year 1950 to 1952, the number of demonstration teams was raised to five and these amply showed that under proper technical direction and control, a substantial lowering of malarial incidence could be achieved by the indoor application of insecticides such as D D T and B H C.

NATIONAL MALARIA CONTROL PROGRAMME

In the year 1952, the total population protected against malaria by the State Malaria Organization was nearly four lacs (0.4 million) which involved an expenditure of nearly Rupees 2,61,000. This inadequacy of the protection afforded against malaria was realized by the Punjab Government early in 1953 when a bold and outstanding decision was taken to participate in the National Malaria Control Programme initiated by the Government of India under the Indo-American Point IV Agreement. During the year 1953-54, the Punjab Government earmarked a sum of Rs 7,47,700 towards this programme and the Government of India's contribution was nearly Rs 11,38,004. This assistance was in the shape of grants of D D T, antimalarials, motor transports and essential spraying equipment provided through the Technical Cooperation Administration. The expenditure on the operational costs was borne by the Punjab Government. In this manner, four malaria control units were created for operation in areas worst affected by malaria in Gurgaon, Karnal, Rohtak, Ambala, Ludhiana, Ferozepore, Gurdaspur, Amritsar and Kangra Districts.

Intensive antimalaria operations consisted chiefly of indoor spraying of village houses with five per cent D D T watery suspension at a dosage of 100 mg per square foot twice during the malaria season. These operations were commenced during July 1953, in nine out of the 13 districts of the State. In the remaining districts routine antimalaria measures were applied by the normal anti epidemic staff on similar lines under the District Medical Officers of Health.

Each malaria control unit consisted of one Medical Malaria Officer (Gazetted), eight Malaria Inspectors, 23 Sanitary Supervisors, 120 Sanitary Beldars (field workers), five Motor drivers, five Cleaners and one Mechanic. In addition, adequate personnel had been provided for the office of each unit at Gurgaon, Karnal, Gurdaspur, and Ferozepore. The mobility of the four Malaria Control Units was ensured by the provision of four trucks and one jeep for each unit.

The programme of work was framed in advance taking into consideration the requirements of the areas to be served. In this manner a total of 8,03,056 rooms in 2,526 villages were sprayed with D D T to afford protection against malaria. In addition antimalaria drugs were administered by these units to 20,142 malaria cases. By the application of these measures nearly 14,00,000 population was directly protected against malaria.

These operations were also extended to deal with community projects of Fandabad, Sonapat, Nilokheri, Jagadhn and Batala, where 2,00,999 persons were

protected against malaria. The community projects, as conceived by the Government of India, have been designed to promote the pre requisite for additional productivity, such as can cater for all the basic elements of rural life.

Assessment of the first year's work under the National Malaria Control Programme in the Punjab indicated that although the target in regard to the total population to be protected could not be reached, still there had been a dramatic effect on the life of the people served by this project. A reduction of 50,000 malaria cases was recorded in the recognized hospitals and dispensaries of areas in the State served by the National Malaria Control Programme. In addition, there was a striking reduction in the spleen and parasite rates amongst the children. Similarly, there was a conspicuous lowering of the population density of mosquitoes.

The outstanding evil influence of malaria is directed towards the great loss of man power in industry and agriculture. The economic gain to the Punjab as it affected the 'Grow More Food' campaign in the year 1953, has been estimated for Karnal and Ferozepore Districts. It has been revealed that there had been an increase of 1,30,562 acres in the area cultivated in three tehsils namely, Karnal, Panipat and Kaithal during the period from July to December 1953 as compared to the preceding year. Similarly, it has been estimated that there has been an increase of 11,327 acres in the area under paddy cultivation alone in three tehsils mentioned above which equals, by a modest official estimate of Rs 126 per acre, to a sum of Rs 14,27,202. This increase in the area under paddy cultivation has been reported only in the case of three tehsils in which intensive antimalaria measures have been carried out during 1953. On the other hand, in Thanesar Tehsil of Karnal District which could not be included in the National Malaria Control Programme there has been a marked reduction in the area under paddy cultivation. Similarly there has been an increase in the area under paddy cultivation in Ferozepore District to the extent of 4,834 acres in 1953 as compared to the previous year which at a modest estimate equals Rs 6,03,084. Similar data is being collected from other districts also and it is expected that the net economic gain to the Punjab would definitely repay to a large extent the expenditure on malaria control programme (Rs 7,47,700) incurred by the Punjab Government during 1953.

Encouraged by the results obtained, the Punjab Government extended their antimalaria programme so as to cover the entire State during the year 1954. For this purpose, seven malaria control units including the existing four units, were raised at an expenditure of nearly Rupees 10.8 lacs (1.08 million). Once again the Government of India, through the Technical Cooperation Mission, agreed to provide the required quantities of DDT, motor transports, essential spraying equipment, etc., at an approximate cost of nearly Rupees 8.5 lacs (0.85 million).

Seven malaria control units were accordingly raised, equipped and trained by June 1954, when intensive antimalaria operations were commenced throughout the State. The disposition of these seven units, total population to be protected and areas to be covered are given below —

Units	Area to be covered (sq miles)	Population to be protected
1 Gurgaon Unit.		
Gurgaon District	1,776 3	7 16,089
Rohtak District	590 0	2 53,911
Karnal Unit.		
Rohtak District	826 6	3,7~ 916
Karnal District	1,726 0	7,22 064
Ambala Unit.		
Karnal District	542 0	1 48 (31)
Ambala District	960 0	4 4 441
Hoshiarpur District	785 0	3 5 449
4 Jullundur Unit.		
Ludhiana District	693 3	3 8 604
Jullundur District	380 1	5 0 1 000
Hoshiarpur District	508 0	1 76
Amritsar District	61 9	4 11
5 Kangra Unit		
Kangra District	70 0	4 11
Gurdaspur District (Pathankot and Gurdaspur Tehsil)	712	1 3 111
6 Gurdaspur Unit		
Gurdaspur District	560 0	3 24 100
Amritsar District	971 0	6 058
7 Ferozepore Unit		
Amritsar District	28 0	13 037
Ferozepore District	2,580 06	7,31 963
Havir District	1,706 0	2 50 000
Total	18,070 20	10,01 118

These units conducted malaria surveys in hitherto uninvestigated areas of State during April and May 1955 and intensive antimalaria operations were commenced during the following month. The technique employed in regard to the functioning of the malaria control units was in conformity with the instructions contained in the 'Operations Guide' issued by the Malaria Institute of India. In

this manner 33,42,333 persons living in 5,868 villages were protected against malaria. In this connection 20,24,400 rooms were sprayed with five per cent D.D.T. twice during the year 1954. In addition

Assessment of the antimalaria work carried out so far has revealed an unprecedented reduction in the number of malaria cases in the Punjab during the year 1954 as compared to the previous years. This is evident from the data reproduced below —

Year	Number of malaria cases recorded in the hospitals and dispensaries of the State
1950	6,80,059
1951	5,11,775
1952	5,16,777
1953	5,08,636
1954	3,80,496

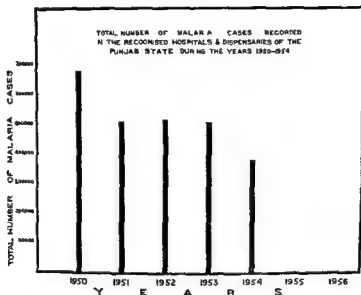
It will be observed that there has been a reduction of nearly 3,00,000 malaria cases had not been the State (Ch

Government dispensaries and hospitals. Considering that a very large number of the affected population do not visit such centres of medical relief, it is expected that the total reduction in the number of malaria cases throughout the State during the whole year must be very great. Similarly reductions in the (i) spleen rates of children (ii) parasite rates, and (iii) number of mosquitoes have been observed (Appendix I)

The transmission of malaria has been considerably reduced as indicated by pronounced lowering of infant parasite rates in all the areas served by the National Malaria Control Programme in the Punjab

From the foregoing account, it is evident that there has been a reduction of nearly 3,00,000 malaria cases during the year 1954 as compared to 1950 when residual insecticides had not been brought into use for malaria control on a very large scale throughout the State. A case of malaria usually incapacitates a person for at least three to six days of his wage earning capacity. At the lowest daily rate now provided by the various Governments, this involves a loss of Rs 12 per head on account of a single attack of malaria. It is, therefore, evident that nearly Rs 36,00,000 were saved in terms of wage earning capacity of 3,00,000 persons protected from attacks of malaria during the second year of the National Malaria Control Programme in the Punjab State,

CHART I.



A substantial reduction in the number of fever deaths has also been reported in the Punjab during the year 1954. The relevant data are given below —

Year	Total number of fever deaths
1950	2,10,961
1951	1,58,871
1952	1,63,140
1953	1,84,858
1954	1,25,005

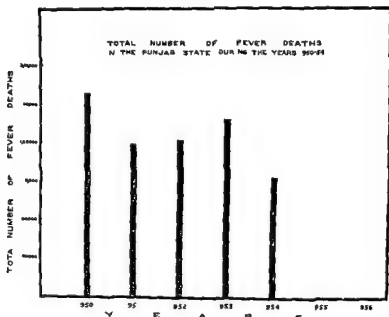
It will thus be observed that there had been a reduction of nearly 85,956 fever deaths in 1954 as compared to the year 1950 (Chart 2)

It is emphasized that apart from other advantages on account of the saving of 85,956 lives, there had been a net saving of Rs 42,97,800 which would have been spent on unprofitable funeral expenses

COLLATERAL BENEFITS

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in the Pur
flea, etc., which are usually abundant. It is also a considerable public yard-stick by which this could be measured except that there is considerable public appreciation in this field as manifested by the growing demand for DDT spray even in areas where malarial incidence is extremely low.

CHART 2



In the Punjab complete control against plague was effected in the year 1950 by the use of residual insecticides chiefly in the indoor rat harbourages. This control has been effectively maintained up till now chiefly by indoor DDT spraying which has been carried out under the National Malaria Control Programme.

The available data also indicate that there has been substantial reduction in the number of total deaths due to diarrhoea and dysentery in Amritsar District since the year 1951 when indoor spraying with DDT and BHC was carried out on a large scale for protecting the population against malaria. The relevant data are reproduced below —

Year	Total deaths due to diarrhoea and dysentery
1942	973
1943	933
1944	915
1945	647
1946	871
1947	1,141
1948	714
1949	619
1950	806
1951	489
1952	441
1953	453

} Mass indoor spraying with residual insecticides

CONCLUSIONS AND SUMMARY

Encouraging results have been achieved during the first two years of the working of the National Malaria Control Programme in the Punjab State

Besides the lowering of malarial incidence there has been considerable saving of human lives. It has also been possible to improve the economic condition of the people by antimalaria operations. A healthy and productive population is the basis of national economic progress which malaria definitely inhibits. The National Malaria Control Programme was introduced at a very critical stage in the political life of the Punjab State which had been badly hit by partition during the year 1947. The alleviation of human suffering by intensive antimalaria operations has to a very large extent been responsible for the upgrading of the economic status of the people.

Judging from the success attained and the progress maintained so far it is expected that the incidence of malaria would be driven to a very low point during the next few years as a result of the National Malaria Control Programme. Having stopped malaria transmission, efforts will be concentrated on strategic control in order that malaria may not reappear.

REFERENCES

- ADAMS J R (1911) *Paludism* 3 p 6
 BAKER J (1916)
 CHRISTOPHERS S R (1911)
 COVELL G (1927) *Ind Med Res Memo* 7
 DEMPSTER T E, BAKER W E and YULE H (1944)
 GILL C A (1914)
 Idem (1915)
 Idem (1917)
 Idem (1920)
 Idem (1921)
 Idem (1923)
 Idem (1924)
 Idem (1928)
 HICKS E P and MAJID S A (1937)
 MACDONALD G and MAJID S A (1931)
 PERRY E L (1911)
 YACOB M and SATYA SWAROOP (1944)
- Govt Printing Punjab*
Malaria in Amritsar Supdt Govt Printing
 Punjab
Ind J Med Res 7, 3 pp 618-630
Ibid 8, 4 pp 673-697
Ibid 11, 2 pp 661-668
Ibid 12, 1 pp 185-194
The genesis of epidemic malaria Baillière Tindall & Cox
 London
Rec Med Surv Ind 7, 1 pp 1-46
Ibid 8, 3 pp 43-48
Paludism 3 p 38
J Mal Inst Ind 5, 3 pp 319-335

APPENDIX I.

Spleen rates amongst children in the Punjab before the National Malaria Control Programme and in November, 1954.

District	Locality	Spleen rate before N M C P (per cent)	Spleen rate in November, 1954 (per cent)
Kangra	Norpur	43 0	5 6
	Shahpur	24 3	16 2
	Jowali	70 1	16 8
	Dera Gopipur	58 0	5 9
	Jowalamukhi	22 0	11 4
	Kulu	33 1	12 0
	Indaura	66 6	14 8
Gurdaspur	Narot Jaamal Singh	28 1	10 8
	Behrampur	51 1	1 0
	Dera Baba Nanak	25 0	2 5
	Siri Gobindpur	27 5	4 8
Amritsar	Patti	70 1	1 1
	Ram Das	27 9	2 9
	Taran Taran	24 5	7 5
	Ajnala	21 6	4 1
	Lopoke	29 8	18 1
	Majitha	21 6	2 9
	Chahal	24 2	3 3
	Amritsar (suburban)	40 5	5 3
Ferozepore	Guru Har Sahai	89 3	3 0
	Zira	49 3	14 2
	Dharamkot	22 1	5 2
Ludhiana	Sidhwan Bet	47 6	2 0
	Machiwara	21 1	7 1
Hoshiarpur	Santokh Garh	31 1	5 3
	Garh Shanker	22 9	4 6
	Hajipur	26 0	21 3
Karnal	Indri	38 0	4 3
	Thanesar	26 9	1 9
	Khojgipur	34 3	4 3
Rohtak	Gohana	23 8	4 6
	Juan	22 9	0 0
Gurgaon	Dhauj	52 8	12 9
	Sohna	35 3	6 4
	Hassanpur	45 2	13 7
	Purahana	59 2	9 4

inert material such as road dust (Barber, 1941b). The use of this mixture became standard procedure and remained so until 1936 when Barber suggested modification—Paris green diluted with oil (kerosene) in the presence of egg album (Barber, 1941c), instead of road dust. When DDT came into prominence it was used in solution with oil (naphtha) to improve the quality of the larvicide (Russell *et al.*, 1946). These, then, were some of the popular materials developed to control mosquito larvae. To distribute these materials, hand equipment of one type or another was used.

Pyrethrins, the toxicant elements in pyrethrum, were first used to destroy adult mosquitoes late in the 1930's (Thornton, 1935). The toxicant was dissolved in kerosene and applied as a space spray. The efficiency of the method was proved in India early in the following decade (Russell *et al.*, 1943), and for a time this spray solution was widely used in spite of its high cost and its lack of residual killing properties.

Pyrethrum space sprays do not compare, though, in overall residual effectiveness, with the newer toxicants represented by chlorinated hydrocarbons commonly referred to as the DDT group. These sprays, properly applied to the resting places of adult mosquitoes, have brought about radically beneficial results in malaria control throughout the world.

Any agent for mosquito control must be applied. Whether the agent is oil, Paris green, pyrethrum, or DDT, it must be distributed by some type of equipment to the resting place of the larvae or the adult. For a long time the development of such equipment was left mostly to chance. Certain types, for instance knapsack sprayers, were taken over from other fields with little attempt to modify them in relation to the new problem. In fact, no active effort was made to develop hand equipment for malaria control until pyrethrum came into use as a space spray. Since

The movement has gained

Health Organization

standardization of hand-operated equipment has rapidly advanced to the point where spray equipment manufacturers everywhere actively seek the Committee's advice.

In the early days of larviciding, when oil was first used, it was apparently applied with any tool at hand. Sometimes the oil was poured directly on the water surface from a container, and spread only because of its repellency toward water. No effort at economy was made, and no spreading agent was knowingly employed. Sprinkling containers of the garden type were frequently used, perhaps the first equipment employed to dispense oil on water as a mosquito control measure. Once malaria transmission had been linked to the mosquito, knapsack sprayers such as those used in agriculture were taken over and used without modification. Throughout practically the entire larviciding era, only slight improvement which could be directly attributed to malaria control influences was made in this apparatus. Even today, wherever the knapsack sprayer is still used it remains the same heavy, cumbersome oiler. No real attempt has ever been made to improve the quality of discharge from the nozzle tip in order to secure better spreading of the larvicide. Actually, little thought was given during the early years to the improvement of larviciding by use of oil, today, because of

the efficiency of other control methods, so little larviciding is carried on that specialized equipment for this means of control is hardly considered necessary.

The knapsack sprayer may be symbolic of all hand larviciding oil equipment. It was pressed into service, performed a useful function without undergoing extensive alteration and has been almost entirely replaced by techniques better suited to the solution of the problem.

When Barber and Hayne developed the technique of destroying *Anopheles* larvae by spreading paris green on water surfaces, they recognized the need for using a very small quantity of paris green per unit of water surface. Consequently a way to dilute paris green had to be devised, and it was necessary to find some inert material with which the toxicant could be mixed. Ordinary road dust became the popular diluent.

It was quite a task to prepare this diluent. First the dust had to be collected, and in malarious areas it was not unusual to see gangs of men along a well travelled highway assiduously collecting road dust. Then the dust had to be screened. An efficient hand operated device was constructed for the purpose. This device was probably one of the first pieces of equipment designed primarily for use in malaria control, another was the mixing drum for combining the dust with the toxicant. Such equipment is now usually found only in museums featuring discarded control methods.

After a proper larviciding mixture of paris green and dust had been prepared it still had to be distributed. A common early method was to put the mixture in a bucket and throw it by hand onto the water surface. Hand bellows to which a small hopper containing the mixture was attached, were also used. A pipe carried the mixture from the hopper to the tip of the bellows, where ejection under low air pressure took place whenever the bellows was operated. This outfit had advantages over hand distribution, but the low capacity of the hopper as well as other drawbacks of a mechanical nature, weighed against great popularity of the apparatus.

Probably the most popular equipment for the distribution of road dust was a type of knapsack duster held on the operator's back with straps. It consisted of a hopper with a capacity of about one cubic foot of mixture and a bellows arrangement, actuated by a hand lever, which pumped air under low pressure and fair volume into a small compartment of the duster. This compartment was automatically refilled with dust. Air pressure agitated the dust. The dust air mixture escaped in uniform quantities. The principle of the apparatus was unchanged. Distributors of this type continued in use in diminishing numbers as long as the road dust paris green technique survived, or until about 1937-38.

Beginning about 1930, demand slowly grew for improved equipment, particularly for hand operated dust distributors with rotary blowers. As with the knapsack larviciding machine, these rotary blowers were borrowed from agriculture and were not efficiently designed. The difficulties experienced in their use were many indeed. Because most of them were badly assembled, they leaked dust through every seam. In addition, little attention had been paid to "balance", with the result that prolonged use tired the operator excessively. Air

passages were not streamlined, this resulted in low-grade dust distribution. Gears and cranks were crudely made. Air-vents and accompanying fans were not constructed to render maximum air delivery with a minimum of effort. One example of such equipment was a square box referred to by the makers as a *venturi*. It was used as a mixing chamber for air and dust. This box, in no sense a *venturi*, frequently became clogged and caused endless trouble. Furthermore, as the operator walked forward to dust a water surface, he had to turn the crank counter clockwise, in order for the apparatus to function at all!

Considerable improvement was made in this type of distributor during the following six or eight years, until the rotary duster was no longer extensively used for malaria control. Possibly due to the need for a better product for malaria operations twenty years ago, this machine is much more substantial and dependable today and is still extensively used in agriculture.

A very important revolution in equipment was brought about after 1936 by the introduction of Barber's wet method of paris green distribution. This method soon eliminated road dust as a diluent. It was no longer necessary to collect, screen, and store vast quantities of dust, nor was it necessary to mix and distribute tons of powder. Instead, an operator carried with him sufficient kerosene paris green mixture to last one day. Water was always available to dilute the mixture to proper proportions.

This system of larviciding required completely different equipment, a type best operated by developing air pressure in the mixture container. The mixture was ejected through a primitive type of nozzle in the form of a spray which readily spread a thin film over the water surface. The apparatus was the forerunner of the hand compression sprayer so extensively used in residual spray operations during recent years. These original hand compression sprayers had mechanical and structural weaknesses, but they were the most efficient tools used for malaria control through the kerosene paris green control period.

Other types of equipment were put into service during the late 1930's and early 1940's. These were, in fact, the real pioneer years for designing equipment adapted to malaria control. Most equipment proved inadequate for the proper distribution of insecticides, however, until about 1940. Since then equipment has been designed more and more to meet this specific problem.

One type of equipment worthy of note for larvicide application was the automatic paris green distributor, a machine originally designed in the Philippines and later perfected in India, which distributed proper quantities of paris green continuously over irrigation canals (Knipe and Russell, 1942). Current in the canals activated the distributor, and the same current carried a charcoal paris green mixture downstream with it, doing a remarkably efficient job of larvæ destruction *en route*. However, popularity of the apparatus waned when the kerosene paris green mixture became popular, even though the equipment could readily be adapted to distribute this material.

northern India in the late 1930's (Covell *et al.*, 1938). Beginning in 1939, an

active field programme - tuted in southern India tiveness of the product were used originally w these cheap sprayers were not well made, did not sufficiently atomize the spray, were small in size, and were inadequately designed. In order to overcome these defects, certain modifications were made: an adequate nozzle tip which assured good atomization was constructed; the container was made of light metal.

This unit was developed in India. It possessed all the qualities of good atomiser. It was widely used in civil organizations and by the army in all continents and in forward areas during war years.

Many other models of sprayers were investigated and developed in this project in southern India. One of these dispersed space sprays through the use of "dry ice" (1942). This was the so-called "dry ice" sprayer.

This unit, which weighed only 28 pounds and was entirely self-contained, was quite efficient. Still another model tried successfully was the prepressurized unit—the prototype of the present day hand compression sprayer. This was pressurized, through a Schrader valve, to 100 pounds per square inch from one of several different sources of air pressure (Knipe and Sitapathy, 1942). A modified Cobra sprayer unit carried the insecticide, which was ejected and atomized by air pressure stored in the hand compression sprayer tank.

At this time the need for some sort of regulator to control pressure on the nozzle tip was recognized, and a lightweight commercial regulator was found which served the purpose.

and Sitapathy, 1942). This regulator was the forerunner of the present-day pressure regulator now advocated for use in one form or another on practically all types of residual spray equipment, whether power driven or hand activated.

popularity of pyrethrum quickly receded.

Residual sprayers as one might expect during the of the new same. The which have sprayers, used practically throughout the world, and the sump-pump sprayer, widely used in India but not to any extent in other countries.

An excellent residue of toxicants may be applied with either type of sprayer. Although the sprayers differ considerably in action, the same amount of insecticide is distributed since distribution is made through the same type of liquid discharge line by each type. Features of this line which have undergone intensive investigation include the following: a bayonet type of attachment (for the hand compression sprayer), a polyvinyl chloride (a plastic), lightweight, highly abrasive resistant hose, a cut off valve which does not leak, a sturdy lance, an automatic non drip valve in the nozzle, and a carefully designed stainless steel nozzle tip which accurately determines the desirable flat spray pattern as well as the rate and angle of discharge.

Since the hand compression sprayer is the type universally used, it has been subject to the greatest improvement. In contrast to its prototype, which was at best, a cheaply designed agricultural tool with many defects, the present day hand compression sprayer is a first class tool for residual spray application and meets practically every requirement demanded of it. This equipment has long since surpassed its predecessor the agricultural sprayer, in quality. Features include an all stainless steel tank construction, welded seams which ensure against leakage, an adequate filler hole which may be semiautomatic in action, a Schrader type filler valve, safety features, plastic leak proof gaskets, a stainless steel lance, a cut off valve, a non drip valve, a nozzle, and a bayonet connection to the liquid discharge line.

These improvements have been made through the cooperation of individuals working on malaria control projects who have consulted with interested equipment manufacturers in several countries. Much of the coordination of details in the programme of development has been carried on by the World Health Organization Committee previously mentioned. This Committee meets from time to time to discuss equipment and to formulate specifications of a general nature which seem to lend themselves to acceptance on a world wide basis.

Hand equipment used in the field of malaria control has indeed passed through an interesting period of development. The early prototypes, borrowed from any available source, served a purpose. They were not always suited to the problem, but successful modifications were usually made. Then specialized models, such as the automatic Paris green distributor, began to appear. Later, types adaptable to pyrethrum distribution were developed and gradually improved with the result that when residual sprays appeared, operators in the malaria control field were fairly well acquainted with the types of equipment required. Models have now been perfected to the point where a malaria officer knows he has dependable equipment with which to carry on his control programme. In fact, spray equipment for malaria control is now of such excellence that technical features are being copied for use in other insect pest control programmes.

The advances made thus far do not mean that the perfect apparatus has been designed. Improvements will continue to be made. Everyone would like to escape the drudgery of pumping or pressurizing, a problem that may be solved by the design of a later control mechanism.

In other words, spray equipment, like most modern equipment, has gone through several periods of development and change. Today's equipment is far superior to yesterday's. The end is still not in sight.

REFERENCES

- BARBER, M. A. (1941a) *A Symposium on Human Malaria Amer Assoc Adv Sci Washington, D C*, p. 337
Ibid, p. 337
Ibid, p. 339
 COVELL, G. MULLIGAN, H. W. and AFRIDI M. H. (1939)
 GINSBURG, J. M. and RUDOLFS W. (1941) *J Mal Inst Ind*, 1, pp. 105-113
A Symposium on Human Malaria Amer Assoc Adv Sci Washington D C, p. 333
 KNIFE F. W. and RUSSELL, P. F. (1942) *Amer J Trop Med* 22, pp. 447-457
 KNIFE F. W. and SITAPATHY, N. R. (1942) *Ibid* 22, pp. 409-416
 RUSSELL, P. F. and KNIFE F. W. (1939) *J Mal Inst Ind*, 2, pp. 209-237
 RUSSELL P. F. KNIFE F. W. and SITAPATHY, N. R. (1943) *Ibid*, 5, pp. 59-66
 RUSSELL P. F. WEST, L. S. and MAXWELL R. D. (1946) *Practical malarology, prepared under the auspices of the Division of Medical Sciences of the National Research Council* p. 440 Saunders Philadelphia
 THORNTON, E. N. (1935) *Ann Rep Dept Pub Health Union of S Africa*, pp. 87-85



ON THE POSSIBILITY OF *A SUNDAICUS* ERADICATION IN INDIA

BY

V VENKAT RAO, FRES, MRSII

(July 15 1955)

THAT it is possible to eradicate vector anophelines from particular areas under certain conditions, and thus to eliminate permanently all chances of malaria transmission there, has been amply borne out by recent work. The eradication measures which have so far been carried out successfully may be broadly classified into three groups as follows —

- (a) Measures dealing with imported vectors,
- (b) Measures carried out in limited areas having natural barriers, and
- (c) Measures where eradication is obtained, not by deliberate action, but rather unexpectedly as a bye product of indoor residual spraying with insecticides

The first concerted attempt at eradication, which falls in the first category mentioned above and which was attended with conspicuous success, was made in Brazil by Soper and Wilson (1943) against *A. gambie* and the next attempt was also made against the same species by Shousha (1948) in Egypt with similar results. These measures involved antilarval as well as anti-adult operations, though it was recognized that the former constituted the primary means of attack with the latter only as supplemental measures wherever necessary. In both cases, Paris green was used against the larvæ and pyrethrum against the adults. Soper and Wilson (1943), however, cautiously observed that their success was due to the fact that the vector was imported into Brazil less than ten years previously and did not yet gain a firm foothold in the country and that *A. gambie*, having selective breeding habits, was more vulnerable to attack than other species which are capable of breeding in a large variety of waters. They doubted whether eradication would ever be possible with autochthonous vector species.

After the advent of DDT, when it became possible to contemplate the elimination of malaria on a global scale, eradication was tried in Cyprus and Sardinia, two small islands in the Mediterranean Sea. Whereas complete success was obtained in Cyprus (Aziz, 1948), the vector of Sardinia has not yet been wholly

eradicated, though it exists in only very small numbers and malaria is brought completely under control (Logan, 1953). In these cases also, anti adult measures were supplemented by antilarval measures.

On the other hand, eradication as a bye-product of indoor residual spraying with D D T has been observed by several workers in various parts of the world. Gabaldon (1949) and Giglioli (1951) have reported the eradication of *A. darlingi* from Venezuela and British Guiana, respectively. Dowling (1951) and Hamon and Dufour (1952) have succeeded in eradicating *A. funestus* from Mauritius and Reunion. *A. sacharovi* has been eliminated from certain parts of Italy (Missiroli, Mosna and Allesandrini, 1948). *A. minimus*, a notorious vector of the Oriental Region, has been virtually eliminated from the sprayed areas of Thailand (Dy, 1954). It should, however, be noted that all these cases have been observed on the border-line areas of the geographical distribution of the species concerned (Gabaldon, 1953).

It, therefore, appears that eradication is possible where the vector is imported into a new region, where the area concerned is limited and bound by

A. sundaicus is a species of the Malayan sub region of zoological distribution and is not properly a member of the Indian anopheline fauna. The only locality in India where it is known to exist with certainty for a long time is the Sunderbans in the deltaic tracts of the rivers Ganges and Brahmaputra (Christophers, 1933) where physical features and ecological conditions are similar to those in the Malayan region. However, its distribution was extended up to the Sunderbans (Gravelly, 1912). In 1933 Budge, only 16 miles from the Sunderbans, it occupied practically the Sunderbans lakes of Calcutta and even extended westward up to about 20 miles from that city. Severe malaria outbreaks occurred in all these areas soon after they were invaded by *sundaicus*.

Another area where *sundaicus* is known to exist is around the Chilka Lake in Orissa, though for how long it has been there cannot be definitely stated. When Hunter (1872) toured the area extensively to prepare a comprehensive report on Orissa to the Government, there was no malaria around the Lake, though Puri Town towards the north and Ganjam Town towards the south of the Lake, were observed to be malarious. However, after a lapse of 40 years, Fry (1912) found an intense degree of malaria infection in the same area, with child spleen rates indicating hyperendemic conditions along the Lake shore. Sarathy (1932) observed similar conditions twenty years later, showing that there was little change in the situation during the intervening period. Though the time of invasion of Puri is not certain, there is some evidence of when the invasion of Ganjam took place. Ganjam is situated about five miles to the south of the Lake. This was a flourishing port and the local headquarters of the East India Company, with a population of 35,000, till 1815, when a violent epidemic of malaria occurred. The

town was then abandoned by the Company and soon became a ruined and insignificant place. If we assume, as perhaps we must, that the malaria in Puri and Ganjam found by Hunter (1872) was due to the presence of *sundaicus*, it was about the year 1815 that *sundaicus* first invaded this area (Senior White and Venkat Rao, 1946). Though the mosquito was present in these two isolated places, it did not extend into the Chilka Lake as long as the Lake had direct access to the sea and its water was too saline for the mosquito to thrive. The subsequent choking up of the outlet and the resultant freshening of the water and the abundant growth of fresh water flora there might, in later years, have facilitated the rapid extension of the mosquito into this area (Venkat Rao, 1949).

The next extension, which was directed southwards, appears to have taken place during or about the year 1930, when violent epidemic exacerbations were reported from Chatrapur Town (five miles south of Ganjam) and from a somewhat extensive area further down the coast known as the "Uddanam", including Naupada, a salt manufacturing centre. Both these areas were previously healthy, having been used as sea side health resorts for a number of years. While, as in the case of Puri (Panigrahi 1942), Chatrapur suffered only from periodical epidemic outbreaks, highly endemic conditions were soon established in the Uddanam area, which became notorious for what came to be known locally as "coastal malaria".

Curiously enough, the latest infiltration to occur was not directed southward along the coast as might have been expected but extended inland up to about twenty miles from the sea, though the worst affected localities were situated within ten miles of the coast. This happened during the years 1942 and 1943 (Senior White *et al.*, 1947).

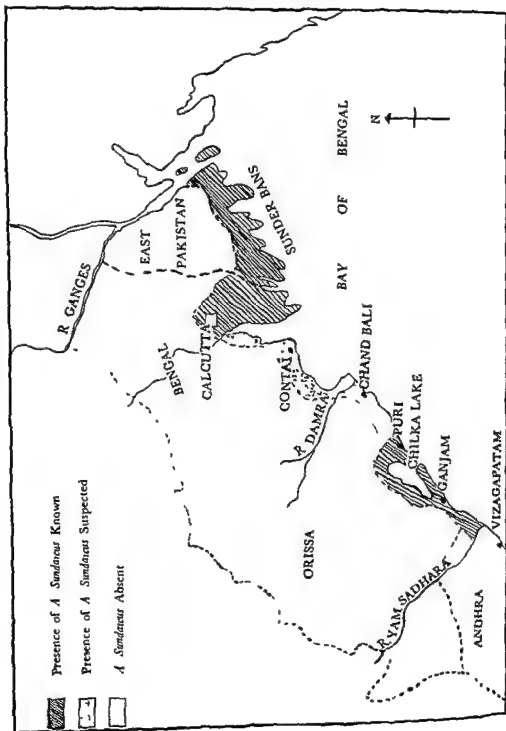
Thus, the areas where *sundaicus* is now known to be present are Lower Bengal, Chilka Lake area and the coastal tracts of Ganjam and North Vizagapatnam districts (Map 1).

The mechanism of extension of this mosquito into Lower Bengal has been described by some authors. After a careful investigation of the means of transport available in Bengal, Sen (1941), observed that, though railway trains were also partly involved, it was the small "country" boats plying the various localities between Sunderbans and Calcutta that were really responsible for the establishment of the mosquito in Calcutta, and that particularly active dispersal occurred during the years 1933 and 1934. This might possibly have been connected with the increased forest fellings followed by rice cultivation near Port Canning (Senior White, 1937).

The first invasion of Puri and Ganjam in the early years of the last century might have been facilitated likewise by small sea going vessels plying between Bengal and Orissa. At that time railways did not exist in India.

It is, however, obvious that the mere availability of railway and boat transport does not by itself result in the expansion of the mosquito into new areas. A number of railway trains run daily between the Chilka Lake and other *sundaicus* infested areas of Orissa, but the mosquito has not spread into these areas.

MAP 1.
North-East India



The invasion of Chatrapur Town, which is only five miles south of Ganjam, occurred over a hundred years after Ganjam was itself invaded, while the area immediately south of Chatrapur remained free from *sundaicus* for at least ten years more. Probably, it is not availability of means of transport but a cataclysmic disturbance like a sudden and unprecedented increase in the population of the species that is responsible for bursts of colonization. Deforestation and extended cultivation near Port Canning referred to above might have resulted in augmentation of breeding places and therefore, in the increase of *sundaicus* population in that area. During 1942, there was an immense increase in the prevalence of *sundaicus* in the Chilka area, pushing up the density in houses to over one hundred per man hour (Venkat Rao *et al.*, 1942). As Senior White (1948) has observed, passive migration may extend the species into new areas but it is likely to die out there, as it did in the areas west of Calcutta.

It is thus shown that, except in the Sunderbans, *sundaicus* is an imported mosquito everywhere else. Except in the isolated localities of Puri and Ganjam where the mosquito appears to have been introduced over a hundred years ago, the importation into the other areas occurred in more recent times, the last burst occurring only about twelve years ago.

Regarding the second postulate, viz., limitation by natural barriers, it is clear that *sundaicus* has a strong predilection for coastal conditions and does not exist far away from coastal and brackish water areas. In Bengal, it has never been found more than six miles from tidal waters (Senior White and Venkat Rao, 1946). Throughout the Chilka area, if isolated collections in small numbers are excluded, the species does not exist beyond a maximum of five miles from the Lake. Further south, including extreme cases, it has never been recorded from places over twenty miles from the Bay of Bengal. It has now disappeared, either spontaneously or as a result of control measures almost entirely from this area.

A *sundaicus* has not been recorded south of the River Vamsadhara. Christophers (1933) referred to *sundaicus* (then known as *ludlowi*) as having been included in the list of Colombo mosquitoes by James in 1914 but it has not since been recorded there and is thought by Carter not to occur in Ceylon.

Thus, the *sundaicus* infested area in the present West Bengal is only about 1,000 sq miles, while in Orissa and North Vizagapatnam areas, the extent is approximately 1,500 sq miles.

The 200-mile length of the coast between Puri and Calcutta has not been surveyed and whether *sundaicus* is present there either continuously or in isolated patches, is completely unknown. The only reference to malaria prevalence in the area is made by Hunter (1872) who says that "fever of low malarious type" is prevalent everywhere and specially so at the mouth of the River Damra, which is about as unhealthy as any found in Bengal and that the malaria season extends from August to October. It is also known that the port of Chandbali is highly malarious. The presence of *sundaicus* may be suspected in both the cases. It, however, appears that continuous distribution of *sundaicus* all along the coast is not very probable as suitable estuarine conditions are seldom found without considerable separatory areas. There are, at least, some known healthy spots on this coast like Contai and Digha. The infested area, if there is any, is thus unlikely

to be more than a thousand square miles in extent, making a total of 3,500 square miles

If *sundaicus* has not extended further inland than it has already done, it is not because of natural barriers but because the mosquito is incapable of doing so owing to its evident need for an equable climate. In fact, the only trait it still exhibits in common with its original home, Indonesia, is its association with the sea shore.

For all practical purposes, therefore, *sundaicus* has a limited distribution and is subject to constitutionally imposed barriers against further expansion inland.

As the presence of *A. sunaicus* has been recorded only on the east coast of India between the Sunderbans and the mouth of the Vamsadhara River and nowhere else, either in India itself or in the countries west of India, it is definite that the area of its present prevalence is the westernmost limit of its area of distribution. *A. sunaicus* here is occupying an extremely narrow marginal zone.

The situation is, however, complicated by the presence, at least in Orissa and North Vizagapatnam areas, of two forms of *sundaicus*, one breeding in fresh waters and the other in saline waters. According to epidemiological evidence, the fresh water form appears to be a potent vector of malaria, while the other form is at best a vector of secondary importance (Senior White *et al.*, 1947).

Now, *sundaicus* has been recognized to be pre eminently a salt water breeder everywhere. The only reference in the previous literature to fresh water *sundaicus* is made by Bonne Wepster and Swellengrebel (1953), who have stated that there was a fresh water form in Sumatra, that it was a potent vector there and that it was eliminated when its breeding places—fresh water fish ponds—were eradicated. Thus, fresh water *sundaicus* appears to have existed in Sumatra and still exists in India, which are the eastern and western margins of the area of *sundaicus* distribution.

The salt water breeding *sundaicus* has always been looked upon as a very effective carrier of malaria in the coastal regions of all countries wherever it occurs. However, Taylor (1943) observed that, owing to the lack of direct correlation between the presence of this species and malaria on all occasions in Singapore it had been thought that *A. sunaicus* of that island might consist of more than one species or variety and that more recent work indicated that this "supposition" was correct. If, as is presumably the case, he referred to salt water breeders only, it appears that, even among them, there are forms which are vectors and others which are not. Even in the Arakan region of Burma, Lalor (1912), Feegrade (1924) and Macan and Watson (quoted by Fox, 1949) dissected altogether 908 specimens with negative results and therefore, *prima facie*, *sundaicus* is not a vector there too. No fresh water breeding has ever been recorded from this area.

The available information indicates that, while there may be, among salt water breeders, some non vector forms, the fresh water forms are potent vectors wherever they exist. Subsequent work carried out by Venkat Rao and his associates in the Godavari delta area has shown that the two forms differ in the number and shape of the setae on the legs, somewhat similar to those observed in the *A. tritaeniorhynchus* complex (Wepster and Swellengrebel, 1953).

It cannot perhaps be assumed that the two forms of *sundaicus* have always been present in this area, the fresh water form, which is located in recent years, should then have evolved out of the earlier salt water form. Huxley (1942) has observed that a single species may separate gradually into two or more divergent lines transcending the limits of species distinction and that the separation into two mutually infertile or otherwise distinct groups may occur suddenly though the subsequent divergence may be gradual. He goes on to state that ecological but spatially overlapping differentiation will promote divergence in general characters since more complete adaptation to two ecological niches will be advantageous to both species. Probably, when *sundaicus* is faced with the problem of heavy overpopulation, it is capable of meeting the situation by separating, more or less suddenly, into two or more groups, each occupying a different ecological zone. When they are thus separated, they may not merge again into one species through cross mating. Though the variations in male genitalia mentioned above may not raise a mechanical barrier to copulation between the sexes of the two forms, there is an imponderable factor of a physiological nature operating against cross mating in such cases (Fennah, 1946). However, as both forms exhibit a marked preference to the ecoclimate of the sea coast and are present together within the same areas, and as both the forms have been found to be vectors in some area or other, this question, so far as eradication is concerned, may not require further discussion.

Having shown that all the three conditions postulated for a successful eradication campaign are satisfied in a large measure in the case of *sundaicus*, the specific measures which should be undertaken for the purpose, shall now be considered:

that eradicate
larvæ and ad
if one has to carry out indoor residual spraying continuously over a number of

(1954) has reported that *sundaicus* in the Djakarta area of Indonesia has developed chemico-resistance against DDT, though not yet to dieldrin, after a few years' spraying indoors. Therefore, as in all other cases where eradication has been purposely aimed at, antilarval measures should constitute the primary means of attack, though indoor spraying should also be pursued simultaneously.

ricefields is minimal, being restricted to the mouths of rivers and the narrow belt of ricefields along the margins of large bodies of saline water like the Chilka Lake. The association of *sundaicus* with aquatic vegetation is very striking and the species will apparently breed in the presence of many different types of vegetation.

While dealing mainly with salt waters, Covell and Singh (1942) have pointed out that it is only when the vegetation comes above the water surface and begins to putrefy that the larvæ of this species are found. This suggests that water

polluted by rotting vegetation favours the breeding. This is in accordance with the observations of Iyengar (1931) that, besides salinity, organic pollution of the breeding place is a cardinal condition of *sundaeus* breeding. Can this be the reason for the poor vectorial status of the salt water form, at least in the Chilka area? The critical experiments of Russell and Mohan (1939, 1940) have shown this to be a wrong premise but Muirhead Thomson (1951) observed that in these experiments the pollution was of animal origin and that it still remained to be seen if gross pollution of the larval environment with vegetable organic matter—a much more widespread phenomenon in nature—would have any effect on the susceptibility of infection of the resulting adults. However, Venkat Rao and Ramakrishna (1947a) have shown that, breeding of the fresh water form occurs in waters which are clear and good enough for the people to use for drinking purposes and that, when the vegetation is removed, the water becomes turbid and polluted and the green alga, *Microcystis aeruginosa* grows in quantities and *sundaeus* disappears. It is thus seen that the salt water form breeds largely in polluted waters and the fresh water form in clean waters, which may be a significant difference in their behaviour.

Covell and Singh (1942) observed the association of *sundaeus* with thirteen types of aquatic plants and eight types of algae, *Najas*, *Ceratophyllum* and *Hydrilla* among plants and *Lyngbya*, *Anabena* and *Spirogyra* among algae being the most important. In fresh waters, association with the same three plants and *Spirogyra* was very marked. Whereas a thick cover of *Eichhornia speciosa* in the breeding place was found to inhibit *sundaeus* breeding in Bengal (Iyengar, 1946).

places both by Covell and Singh (1942) and Venkat Rao and Ramakrishna (1947a).

Control of *sundaeus* breeding may be effected by the use of paris green or naturalistic measures like deweeding. Paris green treatment of the numerous breeding places at intervals of five to six days is a very costly and difficult method. It is also likely to be inefficient during periods of heavy and continuous rainfall. Deweeding thus becomes the only reliable alternative available.

Deweeding by manual and other mechanical means was tried on a large scale in the Chilka and North Vizagapatam areas and proved very effective. The breeding is immediately checked and the breeding places remain negative for *sundaeus* larvae as long as the weed free condition of the water surface is maintained. However, regrowth of vegetation occurs so fast, at least during the first two or three years, that the maintenance work becomes very difficult, requiring a large labour force and proper supervision, without which the work becomes unsatisfactory.

A very much simpler and equally effective method of deweeding is offered by the recent introduction of chemical weed killers. These are claimed to remain effective, after one application, for four to five years, in which case one application may suffice for the whole campaign.

While this method is applicable to inland waters, both fresh and saline, of limited extent, it does not apply, owing to its cost, to the large bodies of salt water like the Chilka Lake, which alone is over 500 square miles in extent. But, in this

lake, though the fauna is marine, the flora is that of fresh water (Annandale and Kemp, 1915), which can be eliminated by raising the salinity through the introduction of sea water. There is a narrow channel in the vicinity of the lake where the water is raised by irrigating the ricefields but fish supply, for which the lake is necessary to keep the mouth of the lake constantly open for the ingress of sea water, as otherwise the littoral sand drift might soon choke the mouth, resulting in the ultimate freshening of water in the lake.

Lastly, effective measures have to be undertaken to prevent re-infestation from the neighbouring countries, East Pakistan and Burma. It is now recognized that, for eradication of malaria or of vector anophelines, international cooperation is essential. The best method would appear to be the application of eradication measures simultaneously in all the three countries.

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REFERENCES.

- ANNANDALE, N and KEMP, S (1915)
 AZIZ, M (1948)
 BONNE WEPSTER, M and SWELLENGREBEL, N H (1933)
 CHRISTOPHER, S R (1931)
 COVELL, G and SINGH, P (1942)
 CRANDELL, H A (1934)
 DOWLING, M A C (1951)
 DY, F J (1954)
 FREGRAPPE, E S (1924)
 FENNELL, R G (1946)
 FOX, D G R (1919)
 FRY, A B (1912)
 GABALDON, A (1949)
 Idem (1953)
 GILFILL, G (1951)
 GRAYFLY, F H (1912)
 HANOV, J and DUFOL, G (1952)
 HUNTER, W W (1972)
 HIXLEY, J (1912)
 IYENGAR, M O T (1931)
 Idem (1916)
 LAJON, N P O'G (1912)
 LOGAN, A (1957)
 MENDICOLI, A, MOSNA, E and ALLESTINDINI, M (1948)
 MEN IND AFUS, 5, p 1
 Proc Fourth International Congress on Malaria, Washington
 The anopheline mosquitoes of the Indo-Australian Region p 400 J H De Bussy, Amsterdam
 Burma
 Proc Ent Soc (1) p 73
 The anopheline mosquitoes of Burma Thesis photostat copy
 First report on malaria in Bengal Bengal Sect Book Depot Calcutta
 Trans Roy Soc Trop Med Hyg 43, p 113
 Rev de Mal 32, p 175
 J Nat Mal Soc 20, p 142
 Rev Ind Afus 7, p 209
 Quoted by Gabaldon 1953
 Uruza Smith Elder & Co, London 2 Vols
 Evolution the modern synthesis p 170 George Allen & Unwin Ltd London
 Ind J Med Res, 19, p 504
 J Nat Inst Ind 6, p 29
 A report on malaria in Kyaukpada Town Govt Press, Rangoon
 Amer J Hyg Monographs Series, 20 Quoted in Trop Dis Bull 32, p 320 (1955)
 Rend d Inst Sup d Sanita, 2, p 759

- MUIRHEAD THOMSON, R C (1951) *Mosquito behaviour*, p 169 Edward Arnold & Co., London
- PANIGRAHI, R G (1942) *J Mal Inst Ind*, 4, p 423
- RUSSELL, P F and MOHAN, B N (1939) *Amer J Hyg*, 30, p 73
- Idem* (1940) *Ibid*, 31, p 19
- SARATHY, M K P (1932) *Ind Med Gaz*, 67, p 254
- SEN, P (1941) *J Bomb Nat Hist Soc* (August 1941)
- SENIOR WHITE, R (1937) *Ind Med Gaz*, 72, p 361
- Idem* (1948) *Ind J Mal*, 2, p 13
- SENIOR WHITE, R and VENKAT RAO, V (1946) *J Mal Inst Ind*, 6, p 297
- SENIOR WHITE, R., RAMAKRISHNA, V and VENKAT RAO, V (1947) *Ind J Mal*, 1, p 81
- SHOUSHA, A T (1948) *Bull World Health Org*, 1, p 303
- SOPER, F L and WILSON, B (1943) *Anopheles gambiae in Brazil*, Rockefeller Foundation. New York
- TAYLOR, F H (1943) *Service Publication No 5*, p 73 School of Public Health Hygiene, Sydney, Australia
- VENKAT RAO, V (1949) *Ind J Mal*, 3, p 313
- VENKAT RAO, V, ROY, B B and JAGAN-NADHA RAO, P (1942) *J Mal Inst Ind*, 4, p 405
- VENKAT RAO, V and RAMAKRISHNA, V (1947a) *Ind J Mal*, 1, p 51
- Idem* (1947b) *Ibid*, 1, p 419
- Idem* (1950) *Ibid*, 4, p 235

SOME MALARIA ERADICATION PROBLEMS AS VISUALIZED IN 1955

BY

F J PAMPANA, M D

(Chief, Malaria Section, World Health Organization)

(August 20, 1955)

¹The ultimate goal of a nation wide malaria control programme is the eradication of the disease —H O Second Asian Malaria Conference, 1954

It seems strange that during the many years of malaria control by residual insecticides so little account has been taken of the destiny of the malaria parasite in man. Attention has been focused on vector control, apparently forgetting that if the vectors have no infection to transmit, their control would be superfluous. The fact that malaria infections die out spontaneously within a few years and that therefore, if no new cases occur or are imported, the population will be cleared of malaria when those few years are over, was very seldom taken into consideration when planning programmes. During the development of a programme, emphasis was put on operational techniques, on the number of houses sprayed, on variations of vector densities, less frequently on those of malarionometric rates, but practically never on achieving the full interruption of transmission which might have led to the eradication of the infection in the population and to the discontinuation of insecticide spraying. This concept was presented as far back as 1948 at the Fourth International Congress of Tropical Medicine and Malaria (Pampana, 1948, 1952), but it was only after the demonstration that some anopheline species could develop resistance to chlorinated hydrocarbon insecticides that it was given serious consideration. It was then felt that resistance was such a danger that efforts should be made to shift the objective of antimalaria activities from simple malaria control, that is reduction of transmission, to malaria eradication, so that residual insecticide applications could be stopped before resistance had a chance to occur (Pampana, 1954). This principle was discussed and a new strategy eventually approved by important international conferences, both at the inter-governmental level (XIV Pan-American Sanitary Conference Santiago, 1954) and at the technical level (Second Asian Malaria Conference, Baguio P I, 1954) and, finally, by the Executive Board (15th Session) of the World Health Organization

in January 1955 and the Eighth World Health Assembly (Mexico, May 1955). While readers of this Journal are probably acquainted with the Report of the Second Asian Malaria Conference, it might be useful to recollect that the Santiago Conference resolved "that it [was] of the utmost urgency that the Member

of nation-wide malaria control so that malaria eradication may be achieved and the regular insecticide-spraying campaigns safely terminated before the potential danger of a development of resistance to insecticides in anopheline vector species materializes." It may be said that there is today a large consensus of expert opinion that wherever it is planned to control malaria by residual insecticide spraying, eradication of the disease should be the goal, so that the insecticide could be discontinued when still fully effective against the vectors. Obviously, eradication

require a larger annual budget than present control programmes, this would only be required for a few years, so that in the end savings would be effected, and (2) that by continuing residual spraying from year to year resistance to the insecticides might develop and malaria control would then become a much more expensive proposition, if not practically impossible

But even malariologists, not to mention public health administrators, may have some doubts as to the advisability, the feasibility and the urgency of malaria eradication. These doubts are quite understandable, for eradication is a new venture. We shall try in this paper to foresee some of these queries and doubts, and attempt to reply.

1. One of the reasons that prompt us to change our strategy is the development of resistance to insecticides. Is it likely that resistance, so far described only in a few species in a few countries or localities, would develop in others? Unfortunately there is perhaps no answer to this first query. But this same question came to the mind of malariologists after the report of the DDT resistance of *A. sacharovi* in Greece (Livadas, 1951, Livadas and Georgopoulos, 1953). Later also in the same country *A. maculipennis* and *A. superpictus* were reported to have developed resistance as well (Belios, 1954). A few months passed. Then in some localities of Java *A. sundaci* it was demonstrated (Crandell, 1954), had become DDT resistant. More months passed, and then resistance was stated to have developed in *A. stephensi* in some localities of Saudi Arabia (Daggy, 1955). If this has happened, it seems reasonable to think that in the future resistance may occur in other parts of the world and with other species. And as resistance to the chlorinated hydrocarbon insecticides might be, in our present state of knowledge, a very serious occurrence in countries which were highly malarious before the inception of control, there is ample justification for adjusting programmes in such a way as to obtain most benefit from the insecticides and to stop their application when they are still active.

2 It is stated that malaria eradication is possible because malaria infections are self curing and do not last more than three years. But we all know of ancient

... nine to twelve months has been in experimental infections with a however 279.5 days (± 19.9) (Je Porto R co t h a t h e n ...)

As regards *vivax* infections which generally do not last beyond two years we shall only recollect observations on infections contracted in the South Pacific in 43 per cent of which clinical attacks were still present four years after (Hill and Amatuzio 1949)

In conclusion there certainly are infections of *P. falciparum* lasting more than one year and of *P. vivax* lasting more than three years. This is a parasitological truth such cases however are rare* and we may assume, for public health purposes that they do not invalidate the general statement that if no new cases of malaria have occurred for three years in a given locality, its population no longer represents a source of infection for anophelines. It should not be forgotten that public health policies are based on generalizations. No vaccination gives 100 per cent protection and still vaccination has succeeded in eradicating smallpox from many a country.

If exceptionally a long lasting malaria infection succeeds in infecting a mosquito and in giving rise to secondary cases the small outbreak could easily be brought under control particularly so if residual insecticides can be effectively employed. It might be compared to an outcrop of secondary cases following the immigration from abroad of a gametocyte carrier such as that described by Brunetti *et al* (1954) in the U.S.A.

3 When could it be stated that malaria eradication has been achieved? We know that among the various malariometric indices the infant parasite rate (IPR) is the most reliable. Figure 1 depicts this example. Of course, a zero infant parasite rate does not necessarily mean that no cases occur in the population,

* In this connexion it may be noted

therefore, we cannot say that malaria eradication has been achieved when we stop the insecticide. It will be necessary first to set up a machinery of searching for the necessary protective measures. This should be set up, as recommended by the necessary protective measures. This should be set up, as recommended by the necessary protective measures. This should be set up, as recommended by the necessary protective measures.

should assume that, as in our figure, it is working already in the year which is supposed to be the last of the spraying years. In other words, in the first example (a) of Figure 1, in the third year of spraying, in the second example (b), in the fourth year. Now let us recollect the definition of the National Malaria Society of the U S A. "Malaria may be assumed to be no longer endemic in any given area when here for three years, if adequate investigations are carried out in the area."

are carried out in the area. This is quoted by the Fifth Report of the Expert Committee on Malaria of W H O. It is that when malaria "is no longer endemic" in any given area, it would mean that eradication had been achieved three years before. In case (a) of Figure 1 eradication would have been obtained in the fourth year, in case (b) in the sixth year. In conclusion the date of actual eradication could only be established retroactively.

4 It has often been recommended that the area of eradication should be "as large as possible" (Reports of the First and of the Second Asian Malaria Conferences). One would think it easier to eradicate malaria from a village or a group of villages rather than from a whole country. But it would be impossible to maintain those localities free of sources of infection for the vector mosquitoes because we can neither compel the villagers to remain for at least three years in their villages, nor preclude the entrance of other people from outside. It might be possible to prevent such exchange of persons if the villages were completely isolated, as, for instance, in the case of an island. With such exceptions, the large size of an area would minimize the danger of sources of infection being imported. The larger the area is, the smaller would be the danger. Eradication on a continental scale, as it has been decided for the Americas, once achieved, will have to establish protection only against travellers coming from other continents or oceanic islands.

Still, in programmes on a continental, sub continental or even country wide scale, it might be expedient and even necessary to proceed by steps and to split the territory from which malaria should be eradicated into zones with different priorities. Each of these zones should, as far as possible, be large enough to reach the borders of healthy areas, or natural, or man made barriers so that the reintroduction of sources of infection would be minimized. In some cases this might not be feasible, and one might suggest continuing the residual spraying of all localities situated at the periphery of the eradication area. But the danger of developing insecticide resistance would counterindicate this idea, which, in any case, would hardly be logical.

5 Still, if the eradication area cannot be surrounded by healthy areas or adequate barriers, some way could be devised to reduce the danger of reintroduction of sources of infection.

Let us suppose that, contiguous to eradication area 'A' is another malarious area 'B' and that the epidemiological conditions in 'A' are such that it can be

FIGURE 1

Tentative schemes of the sequence of events in malaria eradication programmes

Years	-1	1 ^o	2 ^o	3 ^o	4 ^o	5 ^o	6 ^o	7 ^o	8 ^o	9 ^o	10 ^o
Case (a) of conditions exceptionally favourable in which the infant parasite rate in infants born after the first spraying is brought down to naught during the first year											
	SURVEY	ATTACK	CONSOLIDATION			MAINTENANCE					
Spraying operations (on a total coverage base)		XXXXXXXXXXXXXXXXXXXX									
Infant parasite rate	++	o ()	o	o							
Epidemiological surveillance				XXXXXXXXXXXXXXXXXXXX Special surveillance carried out by malaria service				General surveillance carried out by health service			
New cases of malaria locally contracted and traced by epidemiological surveillance				++	o	o	o	↑			
At this point malaria is no longer endemic											
Case (b) of a coverage conditions rather favourable in which the infant parasite rate is brought down to naught only during the second year of spraying											
	SURVEY	ATTACK	CONSOLIDATION			MAINTENANCE					
Spraying operations (on a total coverage base)		XXXXXXXXXXXXXXXXXXXX									
Infant parasite rate	++	++ ()	o	o	o						
Epidemiological surveillance				XXXXXXXXXXXXXXXXXXXX Special surveillance carried out by malaria service				General surveillance carried out by health service			
New cases of malaria locally contracted and traced by epidemiological surveillance	(?)	(?)	(?)	(?)	+	+	o	o	o	↑	

(1) In infants born after first spraying

At this point malaria is no longer endemic

foreseen that spraying can be withheld after four years of operations. It will be recollected that the Second Asian Malaria Conference agreed that "adequate surveillance of malaria incidence should be initiated well before the time of interruption of spraying". Then in area 'A' surveillance should be functioning not later than during the fourth year. Suppose that we provide, in the country-wide programme, for expansion of the operations to area 'B' in this same year. Then a very large proportion of, if not all, new malaria cases in 'B' will be prevented in the year. What will then be the reservoir of infections during the fourth year in 'B'? Very few *falciparum* subjects, infected prior to the spraying, will still show parasites. There will, however, be a good proportion of sources of infections of *P. vivax* and of course of *P. malariae*, contracted chiefly prior to the beginning of

in the fifth year) not many could be capable of infecting the anopheles of 'A'. Moreover, as epidemiological surveillance in 'A' is already functioning, malaria cases both in immigrants from 'B' and in inhabitants of 'A' (who might have become secondarily infected from the former) could be easily traced and dealt with. Finally, if spraying of 'B' in the fourth year reduces, on the one hand, the problem which faces epidemiological surveillance of 'A' it will also, on the other hand, protect visitors from 'A' from getting infected in 'B' and carry back the infection to zone 'A'.

In conclusion, even if no adequate, natural or man-made barrier could be found, it would appear that a satisfactory protection might be secured, if, in a
 tart simultaneously (if not earlier)
 foreseen and if in the same year
 ed

6 As the possibility of starting transmission again after spraying is discontinued appears as a real danger, it would be interesting to visualize how dangerous the immigration of people from malarious areas of varying endemicity into the area from which spraying has been stopped, would be. If we call 'A' the area in which spraying has been stopped, let us call 'B' and 'C' the surrounding areas, which are both malarious. 'B' is hyperendemic, or holoendemic. Everyone of its people will probably be infected, but gametocytes will be found practically only in the blood of children. Now children, introduced in area 'A' would represent a great danger for infecting the local mosquitoes, but children travel much less than adults, and only a few would be likely to be brought into area 'A', moreover, they could be easily spotted, by the surveillance teams, and efficiently treated.

Area 'C' on the other hand, is a mild meso-endemic area, let us suppose with a spleen rate of 20 per cent. Here we would probably find gametocytes carriers among adults, but infected subjects, whatever their age, would represent only a small proportion of the total population. In the cases of both 'B' and 'C', therefore, the danger represented by immigration of people from malarious areas into the adjoining eradication area (if this is sufficiently large and adequately

supervised by epidemiological surveillance) is perhaps less than one would think. The danger would be greater for persons of 'A' visiting 'C' and particularly 'B', but one would think that these persons should they develop malaria upon their return, would more easily be found by the personnel of the epidemiological surveillance and one would count on their willingness to co-operate with them.

The mode of travel across the borders of the eradication area also deserves attention. Travelling on foot, by horse, or ox-cart, by bicycle, etc., represents probably the greatest menace because these are the means employed by rural groups, such as entire families going from village to village. This method of travel however, does not generally cover long distances* and if the eradication area is large enough it would represent a danger only for the peripheral band where epidemiological surveillance should therefore be particularly efficient. Travelling by other means motor bus or train is expensive over long distances. Travelling by other means not travel alone, and the travel of entire families by these means would perhaps not be too frequent and might be restricted to cases of change of residence, important family events etc. Furthermore one would think that most of the people travelling long distances by train would come from towns and go to live in other towns, and towns often have no anophelines or else are the first localities in which malaria is controlled. This reasoning applies even more cogently to those travelling by air.

In conclusion it appears that if the eradication programme covers an area large enough and if epidemiological surveillance is more efficient and strict in the peripheral part of it, the problem of imported gametocyte-carriers could be solved satisfactorily.

7 As shown in Figure 1 it is tentatively assumed that residual spraying may be interrupted obviously with the necessary safeguards after the infant parasite rate has remained at zero for three years. In order to shorten as much as possible the period of years during which insecticide spraying must be carried out, efforts should be made to bring the IPR down to zero rapidly. In WHO's experience this may happen after the first spraying but only exceptionally. More often two years of spraying at least will be necessary. In other cases this is not enough, or in some areas the IPR becomes zero only in some sectors and not in others. Often such failures can be explained by the small size of the area or by disregard of the need of total coverage or by faulty techniques (including for insecticide formulations or rapid sorption of the insecticides by the walls). Should these three mistakes be corrected or avoided and transmission continue then it may be thought that transmission is occurring at least in part outdoors. By repeating the spraying from year to year it is to be expected that the progressive reduction of gametocyte-carriers in the population would eventually stop transmission, but given the advisability of accelerating results with a view to discontinuing spraying before resistance may occur it will be necessary to supplement residual spraying with other anti malaria techniques such as

(a) Anti imago space spraying such as was applied before the DDT era in South Africa in India, in the Netherlands

*It will be noted that in this paper we have refrained from discussing the difficulties caused by nomadism which is a special case and could not be sufficiently dealt with in this way as well.

(b) Larval control, though excluding the use of the chlorinated hydrocarbon insecticides

(c) Use of drugs Very exceptionally would it be possible to submit a whole population of an area to frequently repeated administrations of drugs, for the organization of such schemes would be very difficult and costly, but ways could be found of utilizing the spraying personnel for distributing a few mass treatments to all or to selected groups of the population

The use of drugs might also be considered in areas where the residual insecticide will succeed in fully interrupting transmission, with a view to reducing the number of years during which the insecticide spraying must be continued. It is realized, however, that with the possible exception of Pinotti's (1953) method, the systematic distribution of drugs or a systematic attempt towards radical cure of all cases of *vivax* or *malariae* infections will be a very difficult problem

8 In programmes aiming simply at some degree of malaria control, it is not essential, although desirable, to cover by residual spraying (or possibly to protect by other means) all houses of the area. In programmes aiming at malaria eradication total coverage is essential. Furthermore, if interruption of the spraying is to be applied as soon as possible, not only total coverage will be essential, but also a simultaneous implementation of the programme all over the area, with the same degree of efficiency everywhere (This need of coordination in space, time and efficiency was emphasized in the Report of the Second Asian Malaria Conference). These are, incidentally, the reasons why eradication programmes have a higher *per capita* cost than control programmes. If in some portions of the area people refuse to have their houses sprayed, or if in some
 necessary
 e been
 foreseen had the reaction of the population been more favourable. Hence the need of providing for a suitable education of the population on the one hand, and, on the other hand, for suitable legislation

Legislation for malaria eradication should not only provide authority to overcome the objections of the inhabitants where health education has failed, but, as for instance in countries where the operations are largely decentralized, should also make provision for allowing the central antimalaria organization to intervene if the local authorities are lagging behind the schedule of the national endeavour in which they participate

SUMMARY

As it appears that there is to day a large consensus of expert opinion that the objective of malaria control by residual insecticide spraying should be that of malaria eradication, so that the spraying of insecticide could be discontinued before the local vectors develop resistance to it, some problems related to eradication have been considered. These problems are, whether DDT resistance is likely to develop in future in other species, whether it is correct that from the public health standpoint eradication of the infection can be achieved after a few years,

and when The questions of the size of the area and of the danger of reintroduction of the sources of infection in the area from which malaria has been eradicated, and the influence of the mode of travel on this danger have been considered. Finally, techniques supplementary to insecticide residual spraying are suggested to control pockets where transmission may linger, and the need of adequate legislation in any eradication campaign is emphasized.

REFERENCES

- BELION, G. D. (1954)
 BRUNETTI, ROSEMARY, FIRTZ, R. R. and
 HOLLETT, A. C. (1954)
 CRANDALL, H. A. (1954)
 DAGGY, R. H. (1953)
 HILL, E. and AMATIZIO, D. S. (1949)
 JEFFERY, G. M. and FYLER, D. L. (1954)
 LIVADIS, G. A. (1951)
 LIVADIS, G. A. and GEORGIOPOULOS, G. (1953)
 LOOAY, J. A. (1951)
 MacDONALD, G. (1950)
 PAMPANA, E. J. (1948)
Idem (1952)
Idem (1954)
 PINOTTI, M. (1953)
 SOPER, F. L. and WILSON, D. B. (1943)
Riv. Malar., 33, pp. 33-46
Amer. J. Trop. Med. Hyg., 3, pp. 779-787
Mosquito News, 14, pp. 194-195
Oral communication
Amer. J. Trop. Med., 29, pp. 203-214
Amer. J. Trop. Med. Hyg., 3, pp. 219-224
Unpublished working document WHO/Mal/74
Bull. Wild. Hlth. Org., 8, pp. 497-511
 Quoted from a private communication to
 Dr. P. F. Russell, The Sardinian Project,
 Baltimore, p. 212
Trop. Dis. Bull., 47, pp. 90-915
Proceedings 4th Intern. Congress Trop. Med. and
Malaria, Dept. of State, Washington, D.C.
 Vol. 1, pp. 910-944
J. Amer. Med. Women's Assn., 7, pp. 249-250
Bull. Wild. Hlth. Org., 11, pp. 613-620
Curs. Rendus des 1mes Congres Intern. de Med.
Trop. et du Pal., Istanbul II, pp. 249-256
Anopheles gambiae in Brazil, New York

OBSERVATIONS ON SOME ASPECTS OF THE NOCTURNAL
BEHAVIOUR OF *ANOPHELES CULICIFACIES*

BY

D K. VISWANATHAN,
T RAMACHANDRA RAO

AND

A V HALGERI

(Malaria Organization, Bombay State, Poona)

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INTRODUCTION

This paper reports observations made on some aspects of the nocturnal behaviour of *Anopheles culicifacies*, the most important vector species involved in malaria transmission in India. Such studies throw light not only on the normal pattern of behaviour of the adult mosquitoes but on possible changes which may follow the application of residual insecticides. The insect behaviour vitally affects the degree and duration of successful establishment of malaria control and ultimately, malaria eradication. Insect behaviour not only varies with species as shown by Thomson (1950) in East Africa, Davidson (1953) in Kenya, Wharton (1951) in Malaya and Bordas and Downs (1951) in Mexico, but also with respect to the same species in different geographical areas as shown in the case of *A. fluctulatus* in India, by Nursing, Rao and Sweet (1934) in Mysore, Viswanathan, Ramachandra Rao and Rama Rao (1944) in N. Kanara District (Bombay State), Senior White, Ghosh and Venkat Rao (1945) in Orissa and Jaswant Singh and Mohan (1951) in the Nilgiris (Madras State). *A. culicifacies* is much more widely prevalent in India and transmits malaria in widely separated regions and its pattern of behaviour is, therefore, likely to be more varied. While several studies on certain aspects of the bionomics of adult *A. culicifacies*, such as those relating to resting places, feeding habits, hosts of predilection, longevity, range of flight, ovipositing behaviour, etc., have been published, there are few records on the nocturnal behaviour. Even the few that have been published are based on limited observations (Rajindar Pal, 1945, Rajindar Pal and Sharma, 1952).

METHODS

Two experimental huts were constructed for the purpose of these studies at Vithalwadi located on the banks of the Mutha River, six miles to the west of Poona City. The river bed itself and several small streams, channels and seepages in the locality provided good breeding places for *A. culicifacies*. The huts (Figures 1 and 2) were 8 feet long and 6 feet broad and had gabled roofs, the highest point of which was $7\frac{1}{2}$ feet from the ground. The walls and roof were made of bamboo matting supported by strong bamboos at the corners. The roof was covered by thatch and the inner sides of both the roof and the walls were completely lined with mud plaster. The hut had one door 5 feet \times 2 feet facing east and only one window 1 foot square on the north. The door could be closed fairly tightly. The window was provided on its exterior with an outlet window trap made of cloth netting. On two sides of the hut, across the middle, was a horizontal opening produced by the overlapping of the upper part of the matting over the lower part, the space between the two being about two inches. The extent of the overlap was four inches, and a mosquito in order to enter the hut through these openings had to fly four inches upwards before reaching the interior. When the door was tightly shut, the only entrance available for the mosquitoes was through these long slits. In view of the well known tendency of mosquitoes not to fly downwards when trying to escape, these slits provided possible means of ingress when the door was kept shut but not for their egress. The dimensions of the hut were such that the entire interior could be thoroughly inspected and all resting mosquitoes easily

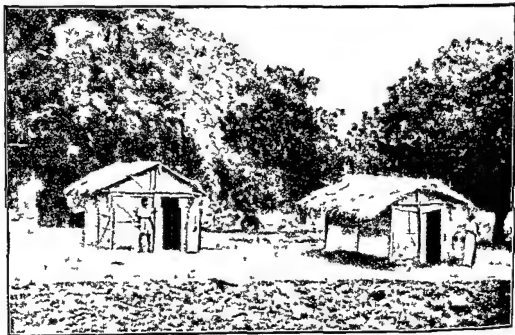


FIG. 1. Experimental huts built for the study of behaviour of *A. culicifacies*.

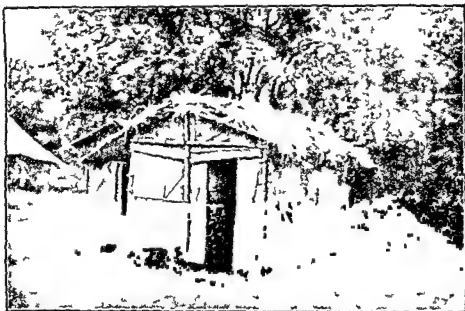


FIG. 2. Closer view of one hut showing the window trap. The arrow points to the slat entrance.

collected by hand with the suction tube. A tent was pitched 50 feet away from the huts to provide a small field laboratory for use at night. Except for a couple of rural houses about 300 yards away there were no other houses within a radius of half a mile.

A buffalo was tethered in the hut between 18.00 and 07.00 hours on every night of observation. Several preliminary attempts with human baits showed

necessary to be able to spot dead insects.

OBSERVATIONS

Observations were made in these huts on the time of entry and the time of feeding from December 1951 to May 1952 and on the effects of DDT spraying in June, November and December 1952. During the monsoon months no observations were made.

MOSQUITO FAUNA

During the course of these studies adults of the following species of mosquitoes were collected in the huts —

<i>Anopheles</i>	1	<i>annularis</i> ,
	2	<i>culicifacies</i> ,
	3	<i>fluvialis</i> ,
	4	<i>hyrcanus</i> ,
	5	<i>jamesi</i> ,
	6	<i>jeyporiensis</i> ,
	7	<i>stephensi</i> ,
	8	<i>splendidus</i> ,
	9	<i>subpictus</i> ,
	10	<i>tessellatus</i> ,
	11	<i>theobaldi</i>
	12	<i>turkhudi</i> , and
	13	<i>vagus</i>
<i>Culex</i>	1	<i>bitaeniorhynchus</i> ,
	2	<i>fatigans</i> , and
	3	<i>tritaeniorhynchus</i>

Further studies were, however, restricted only to *A. culicifacies*

TIME OF ENTRY

In order to determine the time of entry, a thorough search was first made in the huts between 17 30 and 18 00 hours and all resting mosquitoes removed by hand collection. Captures were then made in the huts every three hours by two trained Insect Collectors working simultaneously for thirty minutes, that is, between 20 30 and 21 00 hours, 23 30 and midnight, 02 30 and 03 00 hours and 05 30 and 06 00 hours. Again, a further search was invariably made between 07 00 and 07 30 hours to collect any mosquitoes which had entered the hut subsequent to the search made between 05 30 and 06 00 hours. This time schedule was observed in all seasons of the year.

In a series of 54 observations made with the door fully closed, the total number of *A. culicifacies* collected in these huts was 492 out of which 447 were females (Table I) and in another series of 27 comparative observations made with the door fully open 311 males and 1,118 females of this species, or 1,429 in all, were collected. The figures bring out the fact that nearly five times as many female *A. culicifacies* enter the huts when the door is kept open as when only the slit entrances are available.

Observations made in the three-hourly collections were compared with another series of observations in which catches were made only once between 07 00 and 07 30 hours. The data collected in 18 observations with the door closed and 17 with the door open, are given in Table II. Many of these observations were made on nights alternating with those in which three hourly catches were made and therefore, the data are generally comparable and the seasonal differences in the output from the breeding places do not differently affect the two types of observations. These figures reveal that when the door is kept open, the average number of *A. culicifacies* when only a single collection is made in the morning is

265 females and 116 males as compared with 413 and 116, respectively, when catches are made once in three hours and again in the early morning indicating that most probably a certain proportion—roughly 36 per cent—of *A. culicifacies* females which enter the hut during the night and dawn leave the hut before, say, 1.30 hours. But when the door is kept closed, there is no outward movement during the night as shown by the average number collected in the single early morning catch (113) not being less than the total of all the quarterly collections plus the early morning catch (83). These figures are in accordance with the view that the slit entrances while affording ingress to the mosquitoes are not suitable for their egress.

TABLE I
Number of *A. culicifacies* collected in four 3 hourly collections and at 07.00 hours

Four 3 hourly collections and at 07.00		
Number of nights of observation on December 1951 to May 1952	With door closed.	With door open
Total number of <i>A. culicifacies</i> collected in all the four 3 hourly collections and at 07.00 hours	4	4
Males		
Females		
Average number collected per night	43	
Males	467	211
Females		1114
	0.8	11.6
	8.3	41.3

TABLE II

Number of *A. culicifacies* collected

TABLE II
Number of *A. culicifacies* collected in single catches made at 07.00-07.30 hours

Number of observations		Door closed		Door open	
Total number of <i>A. culicifacies</i> collected in the early morning	Percentage of males	14	15	19	451
Males	13	11.7	11.6		
Females	74	46.5	46.5		
Average number collected per night					
Males					
Females					

Table III are given figures regarding the early morning collection of *A. culicifacies* entering the houses made at 07.00-07.30 A.M.

In Table III are given figures regarding the number and proportions of females of *A. culicifacies* entering the hut at the different quarters of the night

and the early observations study Of it

second quarter, making a total of 90 per cent entering before midnight. Similarly of the 1,118 females collected in 27 nights when the door was kept open, 44 per cent entered in the first quarter and 23 per cent in the second quarter, making total of 67 per cent of entry before midnight. These figures bring out the fact that while *A. culicifacies* enter dwellings throughout the night, the bulk of entry occurs before midnight and that the first quarter is the most active period of entry. The figures further suggest that a certain proportion of those which enter houses in the earlier part of the night, leave them and re-enter later. Thus in the first quarter nearly 30 out of 74 or roughly 40 per cent leave the houses presumably in search of more congenial places of feeding or shelter. In the first and second quarter put together 23 out of 90 or roughly 25 per cent leave the houses. This shows that at least 7 out of the 30 mosquitoes which left the houses out of a batch of 74 which entered during the first quarter, re-entered during the second quarter. Only about ten per cent enter houses for the first time after midnight.

TABLE III

Number and proportions of females of A. culicifacies entering the hut at different quarters of the night and the early morning

	Door closed		Door open	
	24		27	
Number of nights of observations	Number	Per cent	Number	Per cent
Females of <i>A. culicifacies</i> captured in				
1st quarter	320	74	490	44
2nd quarter	1	10	224	23
3rd quarter	9	9	82	"
4th quarter	19	4	121	14
07.00-07.30 hours	19	4	140	12
Total	44	100	1,118	100

TIME OF FEEDING

In Table IV are presented figures showing the proportions of female *A. culicifacies* captured during different times of the night. These figures are based on observations made during the night. The classification of the classes A and B is based on the observations of the classes A and B.

TABLE IV.

Proportions of A. culicifacies females in different gonotrophic conditions

(A) IN COLLECTIONS MADE AT 3 HOURLY INTERVALS AND AT 07.00-07.30 HOURS

Number of nights of observations	Door closed							Door open						
	14							15*						
	Percentages							Percentages						
	Total	1	B	C	D	E	F	Total	1	B	C	D	E	F
1st quarter	319	0	78	12	2	0	2	413	11	56	29	2	0	2
2nd quarter	71	1	83	11	1	0	3	151	7	81	12	0	0	0
3rd quarter	9	0	67	33	0	0	0	30	0	93	7	0	0	0
4th quarter	19	0	68		10	0	10	60	23	15	8	1	0	0
07.00-07.30 hours	19	6	58	10	10	5	0	53	26	41	24	6	0	0
Total	447	3	78	12	3	5	2	716	14	61	22	2	0	2

@ = Less than 1 per cent

(B) IN COLLECTION MADE ONLY AT 07.00-07.30 HOURS

Number of nights of observations	18							-						
	Percentages							Percentages						
	Total	A	B	C	D	E	F	Total	1	B	C	D	E	F
Total	24	2	75	10	3	2	5	137	1	57	41	1	0	0

* Note — The data for nine collections made in May 1952 not included as they are incomplete in respect of gonotrophic conditions

The classification now used is as follows —

- | | | | |
|---------|----------------------|----|---|
| Class A | Empty abdomen, unfed | A1 | With no trace of old blood |
| | | A2 | With traces of previous bloodmeal |
| Class B | Freshly fed | B1 | Fully fed no trace of old blood, or of ovarian development |
| | | B2 | Fully fed with trace of old blood but no ovarian development |
| | | B3 | Fully or partially fed with traces of old partially digested blood and of ovarian development |
| | | B4 | Partially fed without trace of old blood or of ovarian development (interrupted feeding) |

second quarter, making a total of 90 per cent entering before midnight. Similarly, of the 1,118 females collected in 27 nights when the door was kept open, 44 per cent entered during the first quarter, making a total of 88 per cent entering before midnight. This brings out the fact that the bulk of entry occurs during the first quarter of the night. The period of entry of females is thus in the first quarter of the night. Nearly 30 out of 74 or roughly 40 per cent leave the houses presumably in search of more congenial places of feeding or shelter. In the first and second quarters put together 23 out of 90 or roughly 25 per cent leave the houses. This shows that at least 7 out of the 30 mosquitoes which left the houses out of a batch of 74 which entered during the first quarter, re-entered during the second quarter. Only about ten per cent enter houses for the first time after midnight.

TABLE III

Number and proportions of females of A. culicifacies entering the hut at different quarters of the night and the early morning

	Door closed		Door open	
	24		27	
Number of nights of observations	Number	Per cent	Number	Per cent
Females of <i>A. culicifacies</i> captured in				
1st quarter	799	74	490	44
2nd quarter	71	10	254	23
3rd quarter	9	2	83	7
4th quarter	19	4	151	14
07.00-08.30 hours	19	4	140	13
Total	447	100	1,118	100

TIME OF FEEDING

In Table IV are presented figures showing the proportions of female *A. culicifacies* found in different gonotrophic conditions at the time of capture. These are based on the detailed observations on 1,118 females recorded in Table III as detailed observations on 1,118 females in every case. The classification of gonotrophic conditions is the one used by Viswanathan and Ramakrishnan (1944). Her sub-classification of the classes A and B

TABLE IV.

Proportions of A. culicifacies females in different gonotrophic conditions

(4) IN COLLECTIONS MADE AT 3 HOURLY INTERVALS AND AT 07 00-07 30 HOURS

Number of nights of observations	Door closed							Door open						
	54							18*						
	Percentages							Percentages						
	Total	A	B	C	D	E	F	Total	A	B	C	D	E	F
1st quarter	319	6	78	12	2	0	2	443	14	56	29	@	0	@
2nd quarter	71	1	83	11	1	0	3	151	7	81	12	0	0	0
3rd quarter	9	0	67	33	0	0	0	30	0	93	7	0	0	0
4th quarter	19	0	68	5	16	0	10	66	23	68	8	1	0	0
07 00-07 30 hours	19	6	58	16	10	3	0	53	26	44	24	6	0	0
Total	447	5	78	12	3	@	2	716	14	64	22	@	0	@

@ = Less than 1 per cent

(B) IN COLLECTION MADE ONLY AT 07 00 -07 30 HOURS

Number of nights of observations	18							7						
	Percentages							Percentages						
	Total	A	B	C	D	E	F	Total	A	B	C	D	E	F
Total	204	2	76	10	5	2	5	117	1	87	41	1	6	0

*Note — The data for nine collections made in May 1952 not included as they are incomplete in respect of gonotrophic conditions

The classification now used is as follows —

- Class A. Empty abdomen, unfed
- Class B. Freshly fed
- A1 With no trace of old blood.
- A2 With traces of previous bloodmeal
- B1 Fully fed, no trace of old blood, or of ovarian development
- B2 Fully fed, with trace of old blood but no ovarian development
- B3 Fully or partially fed with traces of old partially digested blood and of ovarian development
- B4 Partially fed without trace of old blood or of ovarian development (interrupted feeding)

Class C Partially digested blood
and partial ovarian
development

Class D Gravid, with a slight
trace of old blood

Class E Gravid, without trace
of blood

Class F Miscellaneous

F1 Unclassified

F2 Partial digestion of blood but no
ovarian development

For purpose of Table IV, however, the sub classifications of *A* and *B* are not used

It will be noticed that 78 per cent of all females caught with the door closed and 64 per cent with the door open belong to the Class *B* that is those which had taken fresh bloodmeals. With the door closed, the proportions of specimens

proportion of freshly fed specimens in the first and last quarters than in the second and third. This may be due to the exercise of a greater degree of choice by the mosquitoes resulting in some movement of mosquitoes ready to feed to other possible places of feeding. Altogether while feeding may take place all through the night, generally it occurs soon after entry and as the bulk of the entry takes place before midnight the bulk of feeding also occurs before midnight.

The data also show that a certain number of females in the *C* and *D* classes also enter the huts their total proportions being as much as 15 per cent in the closed door hut and 23 per cent in the open door hut. When a single collection was made at 07.00-07.30 hours their proportions were 15 per cent with the door

in not classes collected been largely restricted to the 07.00-07.30 hours collection, one might have explained it as due to the entry of shelter seekers at daybreak. But the entry of the *C* and *D* classes throughout the night indicates either that there is a

second feeding before their first oviposition. The proportion of the *C* and *D* classes in the open door hut while it is only 15 per cent in the closed door hut while it is only 15 per cent in the closed door hut. Feeding is greater and stimulates entry even with obstacles while the urge for shelter seeking is not so great as to surmount difficulties in entry.

In Table V are given the sub classifications of 1,942 freshly fed *A. culicifacies* (Class *B*) females collected in all the captures made in these huts and in which such data were recorded including also the 447 and 746 females which were dealt with above. Of the 1,942 females subjected to this analysis, 61 per cent were in

B1 condition 19.6 in *B2* 7.1 in *B3* and 12.3 in *B4*. From the details of the classification presented earlier it will be seen that only *B1*, *B2* and *B4* are forms which actually enter the huts in *A* condition that is in an unfed condition with condition and They form meal on the r cent of the ales for the iposed partly in behaviour

are roughly 12 per cent of the again during the same night to complete their bloodmeals. No significant variations in these proportions have been noticed between the different months. The feeding by a proportion of the semi gravid mosquitoes within a gonotrophic cycle somewhat increases Macdonald's (1950) biting index unless in the case of parous females those that bite more than once have their gonotrophic cycle extended at least during that cycle. In the case of nulliparous females the duration between emergence and oviposition is shown by Davidson and Draper (1953) to be at least twice as long as subsequent gonotrophic cycles. Hence the biting frequency is not altered. Multiple feeding in the same night by a mosquito on different hosts profoundly affects transmission the definite extent of which has not yet been precisely determined.

TABLE V

Classification of freshly fed females of A. culicifacies in respect of all collections from January to end of May

Month	<i>B1</i>	<i>B2</i>	<i>B3</i>	<i>B4</i>	Total
January	55	14		11	110
February	181	43	5		301
March	37	4	1	4	394
April	1	11	9	8	81
May	111	1	23	54	301
Total	144	341	134	79	1944
Per cent		6	1	1.3	10

OUTLET WINDOW TRAP

The number of mosquitoes collected in the outlet window traps throughout the period of these studies was very small and extremely disappointing. During the entire period of study with over 200 nights of observations in unsprayed huts only 33 adults of *A. culicifacies* (16 males and 17 females) were found. The outlet window traps were therefore not considered of much utility in the study of behaviour of this species.

DEGREE OF OUT-DOOR RESTING

The observations made in the huts have also not yielded any definite information regarding the degree of outdoor resting during daytime resorted to by adults of *A. culicifacies*. While from a comparison of the number of mosquitoes collected in the three hourly collections and the single collection made in the morning it has been inferred that roughly 36 per cent of *A. culicifacies* leave the dwellings at night, this movement may only be directed towards finding a better place of feeding or shelter. A fair number enter the dwellings in the early morning. Unless the relative numbers which actually leave the huts at night and those which enter the hut in the morning are adequately determined it would not be possible to estimate the proportion which of the relative proportions of early morning collections (T

semi gravid females resting indoors is only slightly less than the number of freshly fed ones and the difference may be due to the natural mortality taking place. It should be remembered that all the mosquitoes reported in these studies were those which entered the hut during single nights, for the huts were thoroughly searched

days cannot be stated. From the first glance of these figures one may conclude that as the gonotrophic cycle is 48 hours practically all the females are endophilic but this will be true only if collections made in dwellings represent the total insect population. Further studies are needed in this regard.

BEHAVIOUR IN HUTS SPRAYED WITH D D T

Several preliminary attempts were made to study the behaviour of mosquitoes in huts treated with D D T. One hut was sprayed on May 23, 1952 at a dosage of 112 mg/sq ft in an aromex water emulsion and observations carried on for 11 nights thereafter till the onset of the monsoon. Collections, made on 11 consecutive nights after the day of spraying, consisted of (i) mosquitoes resting inside the hut (ii) mosquitoes found dead on the floor and (iii) mosquitoes found in the outlet window trap. In all these observations the door was kept closed and only a single collection made at 07.00-07.30 hours. It was soon realized that the number of mosquitoes found dead on the floor did not represent all the dead ones because of the interference by the buffalo which was used as a bait. Therefore, the data in respect of this hut cannot be used for quantitative studies but can be employed for qualitative purposes only. In all these collections only two live *A. culicifacies*,

(1) *Hut sprayed on May 23, 1952*—No separate studies were made in this hut just prior to the spraying but the normal behaviour of the mosquitoes in unsprayed huts as described above, held good. Collections, made on 11 consecutive nights after the day of spraying, consisted of (i) mosquitoes resting inside the hut (ii) mosquitoes found dead on the floor and (iii) mosquitoes found in the outlet window trap. In all these observations the door was kept closed and only a single collection made at 07.00-07.30 hours. It was soon realized that the number of mosquitoes found dead on the floor did not represent all the dead ones because of the interference by the buffalo which was used as a bait. Therefore, the data in respect of this hut cannot be used for quantitative studies but can be employed for qualitative purposes only. In all these collections only two live *A. culicifacies*,

females both in the unfed condition were found resting in the hut. Perhaps they had entered the hut just prior to the collection. Eight males and 12 females of *A. culicifacies* were collected. Of the 12 females 9 were unfed and 3 were fed.

A. culicifacies number of traps excito repellancy but all those which escape death is perhaps insignificant phenomenon of therefore the

(2) *Hut sprayed on November 14 1952*—Preliminary observations were made on four nights before this hut was sprayed in two of which quarterly collections were made and in the other two only a single collection in the morning was made. In all these observations the door was kept open. The results of these collections were as follows

(1) *Single collection at 07 00 07 30 hours*—Two observations—

	Males	Females
<i>A. culicifacies</i>	0	8(B-6, C 2)

(B) *Quarterly collections*—Two observations—

	Males	Females
I quarter —		
<i>A. culicifacies</i>	0	14(A 1 B 11, C 2)
II quarter —		
<i>A. culicifacies</i>	0	3(B 3)
III quarter	Nil	Nil
IV quarter		
07 00 hour	Nil	Nil

After the hut was sprayed collections were made subsequently for six consecutive nights. On these nights collections were continuously made from 18 00 to 24 00 hours and all mosquitoes found resting on the walls or roof caught. The number of *A. culicifacies* and other mosquitoes collected were as follows—

	Males	Females
I quarter —		
<i>A. culicifacies</i>	5	68
All others	2	36
II quarter —		
<i>A. culicifacies</i>	0	0
All others	0	1

The gonotrophic conditions of females of *A. culicifacies* were as follows—

A	B	C	D	E	F	Total
8	58	2	0	0	0	68

These observations are admittedly limited but strongly suggest that *A. culicifacies* do enter D D T sprayed dwellings and take a bloodmeal if facilities for the same are available. Most of the mosquitoes collected at night were, however, found dead before the following midday in the cloth cages to which they were transferred, indicating a high rate of mortality. In the early morning a few dead mosquitoes were also found on the floor but no numerical observations were possible. There were no observations in the outlet window because the door had been kept open.

While our huts proved very useful for the study of certain aspects of nocturnal behaviour, they were not quite satisfactory for the completion of the studies after treatment with D D T mainly because man could not be used as a bait. The buffalo was satisfactory so far as studies in untreated huts were concerned but was most unsatisfactory for studies after treatment. The need now is to find a more 'cooperative' bait or to find a method of restraining the efficient bait in such a manner that it does not spoil the floor and interfere with studies after treatment.

SUMMARY AND CONCLUSIONS

(1) Observations were carried out on the nocturnal behaviour of *A. culicifacies* in two experimental huts constructed for the purpose near Poona City from December 1951 to December 1952 with a break of four months during the monsoon. A buffalo was used as bait for these experiments.

(2) When the only available entrance into the hut was a horizontal slit and the door of the hut was closed, fewer mosquitoes entered the hut for the purpose of feeding or shelter than in a similar hut with the door kept fully open.

(3) *A. culicifacies* enter the dwellings throughout the night but the bulk of the entry takes place before mid night. There was some evidence to show that some mosquitoes which enter in the first quarter of the night leave the dwelling and a smaller proportion amongst them re enter subsequently. Altogether not more than ten per cent of nocturnal entry for the first time takes place after midnight.

(4) Comparing collections made only from 07.30 to 08.00 with collections made from 08.00 to 09.00, 6 per cent of the mosquitoes which entered the hut during the first hour of the night entered during the second hour. It is not, however, possible to say whether such egress is towards outdoor shelters or towards another indoor place either for shelter or for feeding. In other words these experiments do not throw any light on the degree of endophily in respect of *A. culicifacies*.

(5) While feeding occurs all through the night and perhaps relatively early after entry, the bulk of the feeding takes place before midnight because the bulk of the entry also takes place before that time.

(6) When the door is closed and horizontal slits are provided for entry, there is a greater degree of bar to entry of mosquitoes which do not have an urge for feeding. However, even with such obstacles mosquitoes not supposedly in a condition ready for feeding do enter houses during the night. On an average about 23 per cent of mosquitoes which enter at night represent those that are not in a condition ready for feeding.

(7) About seven per cent of the mosquitoes with fresh blood were found with their ovaries half developed and the previous bloodmeal partially digested. As no dissections were made on these mosquitoes it cannot be stated what proportion amongst them represent nulliparous females

(8) About 12 per cent of the mosquitoes which were ready for feeding and which had started feeding showed evidences of interruption. This has a great bearing on the extent of malaria transmission as multiple feeding increases the chances of mosquitoes getting infected on the one hand and transmitting infection on the other

(9) Outlet window traps did not prove successful for the study of the behaviour of *A. culicifacies*

(10) Preliminary observations made on behaviour of mosquitoes in huts treated with D D T showed that it offered no bar to their entry into treated huts and their taking a bloodmeal. There is a very slight evidence of an excito repellent mechanism after contact with treated surfaces but on the whole even those which were excited and repelled have apparently picked up sufficient dose of insecticide to be lethal

REFERENCES

- BORDAS E and DOWNS E G (1951) Control of *Anopheles pseudopunctipennis* in Mexico with D D T residual sprays applied in buildings. Part IV. Activity pattern of adult *A. pseudopunctipennis* Theor Amer J Hyg 53, pp 217-3
- DAVIDSON G (1953) Experiments of the effect of residual insecticides in houses against *Anopheles gambiae* and *A. funestus* Bull Ent Res 44 pp 231-254
- DAVIDSON G and DRAPER C C (1953) Field studies of some of the basic factors concerned in the transmission of malaria Trans Roy Soc Trop Med Hyg 47, pp 572-580
- JASWANT SINGH and MOHAN B N (1951) Studies on nocturnal activities in *A. fl. asiaticus* James 1902 Ind J Mal 5 pp 513-520
- MACDONALD G (1950) Analysis of malaria parasite rates in infants Trop Dis Bull 47, pp 915-938
- NURNING D, RAO B A and SWEET W C (1954)
- RAJINDAR PAL (1945) Behaviour of mosquitoes in relation to insecticidal applications Ind J Mal 6, pp 217-235
- RAJINDAR PAL and SHARMA M I D (1952) Behaviour of mosquitoes in relation to insecticidal applications Ind J Mal 6, pp 281-301
- SENIOR WHITE R, GHOSH A R and VENKAT RAO V (1945) On the adult bionomics of some Indian anophelines with special reference to malaria control by pyrethrum spraying
- THOMSON R C, MUIRHEAD (1940)

VISWANATHAN, D. K., RAMACHANDRA RAO, T.
and RAMA RAO, T. S. (1944)

The behaviour of *Anopheles fluviatilis*
Part II Nocturnal movements and day time
resting places and their bearing on spray
killing

J. Mal. Inst. Ind., 5, pp. 449-461

WHARION, R. H. (1951)

Habits of adult mosquitoes in Malaya

I Observations on anophelines in window trap
huts and at cattle sheds *Ann. Trop. Med.*, 45,
pp. 141-154

MALARIA CONTROL BY THE USE OF INSECTICIDES

A Global Review.

BY

RAJINDAR PAL

AND

M I D SHARMA

(*Malaria Institute of India Delhi*)

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INTRODUCTION

THE advent of insecticides has marked a new stage in the long history of malaria as their application has demonstrated unprecedented success in the control of this disease and the economic feasibility of nation wide control programmes throughout the world. Pyrethrum sprays were introduced on a large scale in 1937 followed later in 1945 by the synthetic insecticides. The object of this paper is chiefly to review up to date observations made on the use of insecticides in malaria control and particularly their effect on the vector anopheline mosquitoes in different parts of the world*. This has helped to point out certain lacunae in our knowledge in respect of some of the species. It is hoped that the review will be of some use as a ready reference to the workers in the field.

RATIONALE OF THE METHOD—THEORETICAL CONSIDERATIONS

It is well known that the mosquito is a vector of malaria. It could be achieved by reducing the number of vector anopheline below a certain figure

*The results in term of malaria control have already been admirably summarized by Summons and Uphoff (1951) Pampana (1951) and Russell (1952a)

which was referred to as the critical density of the vector species. With the introduction of insecticides, however, a new concept has been put forward that even in the absence of mosquito reduction, malaria reduction can be achieved through interception of the vector. A mosquito is able to transmit malaria only ten to twelve days after taking an infected blood feed. If this mosquito could be destroyed before the parasite had time to develop to the infective stage, transmission of malaria would not be possible. The reduction in the longevity of mosquitoes is achieved through any of the adulticidal methods whether by space or residual spraying.

Precise selection of insecticides has on the mosquito treated surfaces. They are grouped as

- (a) *Indoor biters and indoor resters* which are most associated with man and are consequently the best malaria vectors
- (b) *Indoor biters and outdoor resters*
- (c) *Outdoor biters and indoor resters*—Both (b) and (c) have varying degree of association with man and are consequently malaria vectors of secondary importance
- (d) *Outdoor biters and outdoor resters* which are the least associated with man and are consequently less important in malaria transmission

It would be obvious that mosquitoes in groups (a) and (b) have the best chances of contact with the treated surfaces as they rest or feed indoors, thereby coming into contact with the treated surfaces. In the third group, the mosquitoes may come into contact with the treated surface if they rest in houses after the feed, thus giving a varying degree of malaria control, whereas in the fourth group control by the application of insecticides may not at all be possible.

In the first group of mosquitoes reduction or near eradication of the vector may result whereas in the other groups, there may or may not be appreciable reduction in mosquito density although malaria control may be achieved through interception of the vector anopheline.

These statements are however, oversimplified because whether the species is a zoophilic or anthropophilic and what percentage of the mosquitoes rest indoors or outdoors would affect their control by the application of residual insecticides inside the houses.

PRACTICAL RESULTS ACHIEVED

One thing is clear that the application of insecticides has a profound effect on the control of malaria under widely different conditions. Malaria reduction to a greater or lesser degree has followed premises spraying with residual insecticides wherever it has been efficiently carried out in spite of the diversified habits of the vector species. A good example may be cited of the two most notorious vectors of malaria in India, *A. culicifacies* is a domestic species with large numerical prevalence, predominantly zoophilic with poor infectivity rate and on the contrary *A. fluviatilis* is a sparse species resting mostly outdoors, predominantly anthropophilic.

with high sporozoite rate, yet malaria transmitted by both has been equally well controlled. There are, however, a few exceptions where malaria control may be doubtful due to one or the other of the following factors—

- (i) *Due to the peculiar habits of the vector species*—The mosquitoes belonging to group (d) mentioned above may not be vulnerable to this method of attack. Gabaldon (1953a) has made reference to failure of malaria control with residual insecticides in case of *A. bellator* in Trinidad, and also *A. minimus flavirostris* in Philippines. The malaria transmitted by the former species in Brazil and the latter species in parts of Philippines has, however, been controlled to a certain degree.
- (ii) *Due to the repellent effect of residual insecticides*—For example *A. gambiae* and *A. melas* in Africa are repelled by DDT but are successfully controlled by BHC. In the oriental region, Bertram (1951) reported unsuccessful results with DDT on *A. minimus* in Assam and Reid (1951) on *A. letifer*. These findings have not been supported by other workers—Dowling (1951) Hamon and Dufour (1952) as quoted by Gabaldon (1953a) in the case of *A. gambiae*. Gilrov (1951) in the case of *A. minimus* and Nair (1951) in the case of *A. letifer*.
- (iii) *Due to the development of resistance to residual insecticides*—The development of resistance in vector species may jeopardize control of malaria. So far only a few authentic cases of resistance have been reported namely *A. sacharovi* in Greece, *A. albimanus* in Panama and *A. sundatus* in Indonesia but not to an extent sufficient to interfere very seriously with control programmes.

Near eradication of malaria has been reported in the case of *A. quadrimaculatus** in U.S.A., *A. darlingi* and *A. albimanus* in Venezuela. *A. fluviatilis* in Bombay State India. On the contrary only slight reduction in malaria has been achieved in the case of following species *A. aquasalis* in South America *A. testipennis* in Mexico *A. sacharovi*, *A. sergenti* and *A. superpictus* in Jordan. *A. mouchei mouchei* in Belgian Congo, *A. albimanus* in Mexico.

It would also be obvious from the following pages that uniform results on the same vector species in different areas have not been obtained perhaps due to the varying degree of efficiency with which control programme has been carried out, the differences in the habits of the same species in different areas and other local factors and circumstances.

The disparity in the results obtained with different vector species with similar resting and feeding habits is however not clear unless it could be shown that in details the habits were variable. Presumably the disparity may be due to the varying proportion of indoor and outdoor resters and biters and whether zoophilic or anthropophilic. It would be evident that in case of all the seven species referred to above where only slight reduction of malaria has been reported there are local variations in their resting and feeding habits and food preferences.

It may, however, be pointed out that in spite of the fact that insecticides have been used for the control of malaria for about ten years there are a number of species about which no data is available (Table I). It would seem desirable that investigations on these species should be given priority.

* formerly marked acquired resistance has been reported in the case of *A. quadrimaculatus* in certain parts of U.S.A. (Personal communication—H. D. Quarterman 1955)

TABLE I

LIST OF SPECIES ON WHICH DATA IS NOT AVAILABLE

and *A. tessellatus*

The actual results achieved in the field on the effect of insecticides on vector anopheline mosquitoes are briefly summarized in the following pages. The data on the resting and feeding habits of mosquitoes and their sphere of influence has also been included *

GROUP (A)

INDOOR BITERS AND INDOOR RESTERS

1. *A. (M.) aconitus* Donitz, 1902 — Vector in Indonesia and Indo China

Adult females, as a rule, feed and rest indoors. They readily feed on man. Anthropophilic indices of 11.2 (caught from houses) and 0.5 (caught from stables) per cent have been recorded from Indo China and 12.0 (cattle present) and 61.0 (cattle scarce) per cent from Indonesia.

In Indonesia, Van Goor and Lodens (1952) reported reduction in the vector population and malaria morbidity with D D T residual spray applied at the rate of 200 mg/sq ft

2. *A. (N.) albularsis* Lynch Arribalzaga, 1878.—Vector in Brazil, Columbia and Venezuela

Adults in certain areas may occur in houses and show marked preference for human blood, in other areas they do not appear to occur in houses, and they may have preference for animal blood.

In Venezuela, Gabaldon and Berti (1954) have reported malaria eradication Pinotti (1951) in Brazil, reported reduction in malaria morbidity with DDT, residual spray applied at the rate of 200 mg/sq ft though there was no effect on the vector density.

3 *A. (M.) annularis* Van der Wulp, 1884 — Vector in Eastern India, Pakistan and Burma

Adults are found in large numbers in cattle sheds, and sometimes in houses also. Usually they feed and rest indoors. They are markedly zoophilic but feed on man as well. Anthropophilic indices of 10.0 (cattle present) and 50.0

*Publications by Covell (1927-1931), Russell *et al* (1943-1948), Bond (1949) Russell (1955) and Gabaldon (1958) have been freely consulted

(cattle scarce) per cent have been recorded from Indonesia and 16 per cent from Assam, India

In India, Hajra (1948) and Adhikari and Ganguli (1949) recorded reduction in the vector density and malaria morbidity with DDT residual spray applied at the rate of 38-50 mg/sq ft

4 *A (N) aquasalis* Curry, 1932 — Vector in Venezuela, Brazil, Trinidad, Grenada and Santa Lucia

Adults in some localities are anthropophilic and house frequenting and in other zoophilic and sylvan. Zoophilic species seldom found in houses when domestic animals are abundant. Its vectorial activities may be limited because of this fact

In Brazil, Trinidad, Tobago and Venezuela, Pinnotti (1951) and Gillette (1953) recorded reduction in malaria morbidity with DDT residual spray applied at the rate of 200 mg/sq ft, though there was no effect on the vector density. Senior White (1951) has observed in Trinidad that *A. aquasalis*, an indoor refter, has been found resting outdoors

5 *A (A) atroparvus* Van Thiel, 1927 — Vector in Baltic, Netherlands, Germany, Portugal, Spain and Rumania

Domestic mosquito, spends most of its life indoors, is powerfully attracted to stabled animals almost to the exclusion of man, but may overflow into human habitations in search of food under various circumstances, among which are disproportionate density of anophelines or scarcity of animals or for other reasons connected possibly with temperature, humidity or odour. Although bites man less readily, yet anthropophilic indices 6.09 and 40.0 per cent in Spain and 84 per cent in Holland have been recorded

In Netherlands, Van Thiel (1953) as quoted by Gabaldon (1953a, 1953b), recorded reduction in vector density and malaria morbidity with DDT residual spray applied at the rate of 100-200 mg/sq ft

6 *A (A) aztecus* Hoffman, 1935 — Vector in Mexico

Adults feed indoors as a rule. Feed on man or animal without much preference. Rest indoors as well as outdoors

In Mexico, Downs and Bordas (1951) reported reduction in malaria morbidity with DDT residual spray applied at the rate of 200 mg/sq ft

7 *A (A) claviger* — Vector in the Near East, Baku Region, Cyprus and Palestine

A domestic species in Palestine, where it commonly enters houses and freely bites human beings and rests in indoor shelters. In some countries it is considered to be wild species and it rarely enters houses

In Greece and Italy, Livadas (1950) and Missiroli *et al* (1948) recorded reduction in malaria morbidity with DDT residual spray applied at the rate of 180-200 mg/sq ft. They did not observe any effect on the vector density

8 *A (K) cruzi* Dyar and Knab, 1908 —Vector in South East Brazil

Adults feed and rest indoors and outdoors and prefer animal blood

In Brazil, Pinnotti (1951) observed no effect on vector density but there was reduction in malaria morbidity with D D T residual spray applied at the rate of 200 mg /sq ft

9 *A (M) culicifacies* Giles, 1901 —It is an important vector in India, West Pakistan, Afghanistan, Ceylon and Burma

Adult females feed and rest indoors and they bite man freely but the anthropophilic index is usually low, except during an epidemic. Anthropophilic indices of 1.6 and 2.5 per cent have been recorded from India

In India, reduction in vector density and malaria morbidity was recorded by the application of D D T at 50-60 mg /sq ft and of B H C at 10 mg gamma isomer/sq ft (Jaswant Singh and Dalip Singh, 1949, Viswanathan, 1950, Jaswant Singh *et al*, 1951). Similar results were obtained in Pakistan and Ceylon with D D T applications at 25-38 mg /sq ft (Afridi and Bhatia, 1947, Puri and Bhatia, 1947) and 50-200 mg /sq ft (Rajendram and Jayewickreme, 1947) respectively

10 *A (N) darlingi* Root, 1926 —Vector in British Honduras, Columbia, Venezuela, Guianas, Brazil, North West Argentine, Bolivian foot hills, Ecuador and Peru

This species is markedly anthropophilic, and readily enters houses from dusk to any time at night. As a rule, rests in indoor shelters. In Venezuela, out of 100 mosquitoes of this species caught 90 to 98 were from human dwellings. Anthropophilic index of 63 per cent has been recorded from Brazil

In Brazil, with D D T (200 mg /sq ft) application though there was little effect on vector density, there was reduction in malaria morbidity (Pinnotti, 1951). Similar applications of D D T in Argentina and French Guiana also resulted in reduction in malaria morbidity (Alvarado 1953, as quoted by Gabaldon 1953a, 1953b, and Floch 1952). There was reduction or eradication of the vector as well as malaria in Bolivia (Moscoso Carrasco, 1953, as quoted by Gabaldon, 1953a, 1953b) and Columbia (Ranjifo and de Zulueta 1952) and in Venezuela with D D T applications at 200 mg /sq ft

11 *A (M) farauti* Lavern, 1902 —Vector in Australia, New Guinea, Solomons, Hebrides, New Britain to Eastern Celebes

Adult females may feed and rest indoors or outdoors and take human or cattle blood without much preference

In New Hebrides islands and New Guinea, reduction in vector density and malaria morbidity was recorded with D D T application at the rate of 100 mg /sq ft (Yust, 1947, and Bang *et al*, 1947)

12 *A (A) freeborni* Aitken, 1939 —Vector in West U S A, and North West Mexico

Adults feed and rest indoors. They readily feed on man, show progressively higher prevalence of human, pig, horse and cattle blood in their precipitin tested

stomach contents Malaria has practically disappeared in territories occupied by this vector (Hackett, 1952)

¹³ *A (M) funestus funestus* Giles, 1900—Vector in East, West, Central and South Africa Mauritius and Madagascar

Adult females feed and rest indoors and are anthropophilic It has been shown that the species prefers to bite indoors and that an increase in number of occupants in a hut causes an increase in the number of adult mosquitoes which enter it Anthropophilic index of 61.3 per cent has been recorded in Kenya

Reduction in malaria was observed in Southern Rhodesia (Ahes 1951) with BHC (45 mg gamma isomer/sq ft) and in Ruanda Urundi (Jadin, 1951) with DDT (200 mg/sq ft) application Eradication and reduction of the vector and reduction in malaria morbidity has been recorded in Mauritius (DDT 170-260 mg/sq ft), Reunion and Belgian Congo (DDT 200 mg/sq ft) with DDT applications (Dowling, 1951, Hamon and Dufour 1952 as quoted by Gabaldon 1953a 1953b and Vincke 1948) There is a very remarkable control scheme in Madagascar, larger than any of the others in which local eradication of this species has been obtained together with *A gambiae* (Personal communication from Prof G Macdonald, 1954)

¹⁴ *A (M) gambiae gambiae* Giles 1900—Vector in East West Central and South Africa, Mauritius, Madagascar and Reunion

Adult females feed and rest indoors and definitely prefer human blood High anthropophilic indices of about 82 per cent have been recorded from West Africa Jadin (1951) in Ruanda Urundi observed reduction in malaria morbidity with DDT (200 mg/sq ft) application Dowling (1951) in Mauritius (DDT 170-260 mg/sq ft), Hamon and Dufour (1952) as quoted by Gabaldon (1953a 1953b) in Reunion and Vincke (1948) in Belgian Congo (DDT 200 mg/sq ft) observed that there was no effect on vector density though there was reduction in malaria morbidity with insecticidal applications

¹⁵ *A (M) gambiae melas* Theobald 1903—Vector in West Africa (coastal zone)

It feeds and rests indoors and prefers human blood Data on its control by the use of insecticides not available

¹⁶ *A (M) hancocki* Edwards 1929—Vector in East, West and Central Africa

It feeds and rests indoors and takes human or animal blood without much preference Data on its control by the use of insecticides not available

¹⁷ *A (A) hyrcanus sinensis* Wiedemann 1928—Vector in the plains of China and Formosa

It feeds and rests indoors and takes human or cattle blood without much preference In parts of China, it is a voracious human feeder Anthropophilic indices as high as 95 per cent and as low as 0.9 per cent have been recorded from Shanghai and Indo-China, respectively

Reduction in vector density was recorded in Nanking Region, China, with D D T applied at the rate of 150 mg /sq ft (*Agr Res Council Abstracts*, 1950, as quoted by Jaswant Singh *et al*, 1954)

18 *A (M) Jeyporiensis candidiensis* Koidzumi, 1924 —Vector in Travancore (India), Burma, Indo China and South China

Adult females feed indoors but may rest indoors or outdoors and are strongly anthropophilic. Anthropophilic indices of 59.0 and 70.0 per cent have been recorded from Indo China.

Data on its control by the use of insecticides not available

19 *A (M) kochi* Donitz, 1901 —Vector in Indonesia. Adults are moderately domestic, frequenting houses and stables and feeding on man and animals.

Data on its control by the use of insecticides not available

20 *A (A) labranthæ* Falleroni, 1926 —Vector in Spain, Morocco, Algeria, Tunisia, Italy, Corsica, Sardinia and Sicily

Adult females enter houses in large numbers. They are not known anywhere to be effectively deviated from man by domestic animals. They prefer to feed, rest and hibernate in buildings. This makes house spraying with insecticides specially effective.

In Italy Missiroli *et al* (1948) reported reduction in vector density and malaria morbidity with D D T (200 mg /sq ft) residual spray.

21 *A (A) maculipennis maculipennis* Meigen, 1818 —Vector in Turkey and Bulgaria

Adult females feed and rest indoors and outdoors and prefer animal blood but at times may feed on man.

Livadas (1950) recorded reduction and eradication of vector and reduction in malaria morbidity in Greece with D D T (180 mg /sq ft) residual spray. Missiroli *et al* (1948) in Italy observed reduction in malaria morbidity but little effect on vector density with D D T applied at the rate of 200 mg /sq ft.

22 *A (M) mangynus* Banks 1906 —Vector in Philippines

It bites indoors but may rest indoors or outdoors.

In Philippines Bhatia (1953) as quoted by Jaswant Singh *et al* (1954) recorded reduction in its density with D D T applied at the rate of 200 mg /sq ft.

23 *A (A) messæ* Falleroni 1926 —Vector in Hungary, Germany, Poland U S S R, Balkans and Manchuria

It is powerfully attracted to stabled animals almost to the exclusion of man, but may overflow into human habitation in search of food under various circumstances among which are a disproportionate density of anophelines or scarcity of animals, or for other reasons connected possibly with temperature, humidity or odour. Anthropophilic index of 63.0 per cent has been recorded in Holland.

In Netherlands, Cséh Firtos (1952) recorded reduction in vector density and malaria morbidity with D D T residual spray applied at the rate of 200-300 mg /sq ft.

24 *A (M) minimus minimus*—Vector in North east India Burma, Indo-China South China, Formosa, Indonesia, Hong Kong, Thailand, Amoy Island, Sumatra, Celebes and Moluccas

Mainly a domestic species with a high preference for human blood. It feeds indoors but may rest indoors or outdoors. Anthropophilic indices as high as 85.7 and 92.4 per cent have been recorded from India.

In India, DDT applied at the rate of 50-120 mg/sq ft (Puri and Krishnaswami, 1947, Kar, 1950, and Krishnaswami 1952) and in Thailand at 100 mg/sq ft (Bhatia, 1953, as quoted by Jaswant Singh *et al*, 1954) resulted in reduction of vector density and malaria morbidity.

25 *A (M) moucheti moucheti* Evans 1925—Vector in Belgian Congo and Uganda. It feeds and rests indoors and takes human or animal blood without much preference.

Davidson (1950) as quoted by Gabaldon (1953a, 1953b) recorded slight reduction in malaria morbidity with BHC applied at the rate of 10 mg gamma isomer/sq ft.

26 *A (M) moucheti nigeriensis* Evans 1931—Vector in Nigeria. It feeds and rests indoors and takes human or animal blood without much preference. Data on its control by the use of insecticides not available.

27 *A (M) nili* Theobald, 1901—Vector in Belgian Congo Liberia, Sierra Leone. In some parts, this species enters houses bites man and may be an important vector of malaria, whereas in others the insect is rare and is of no importance.

Data on its control by the use of insecticides not available.

28 *A (M) philippinensis* Ludlow, 1902—Vector in Bengal India and East Pakistan. Adults chiefly rest in houses usually 1½ ft off the floor, biting at night between 8 p.m. and 4 a.m. In Assam this species appears to be zoophilic. An anthropophilic index of 6.4 per cent has been recorded from Assam, India.

In East Pakistan, Nasir ud din (1952) recorded reduction in malaria morbidity with DDT applied at the rate of 106 mg/sq ft.

29 *A (A) pseudopunctipennis* Theobald 1901—Vector in Mexico, Colombia, Bolivia Peru Chile, Argentina probably Guatemala, Venezuela and Ecuador.

As a rule, adult females feed and rest indoors and take human or animal blood without much preference. Anthropophilic indices of 50 to 67.6 per cent in Argentina and 2.5 per cent in Venezuela have been recorded.

In Mexico, Downs *et al* (1950) observed reduction in vector density and malaria morbidity with DDT application (200 mg/sq ft). Similarly DDT (200 mg/sq ft) residual spray in Colombia Ecuador, Peru (Montahan, 1953) and Argentina (Alvarado, 1953 as quoted by Gabaldon, 1953a, 1953b) resulted

in the reduction of malaria morbidity. In Bolivia and Venezuela, D D T. applied at the rate of 200 mg /sq ft reduced malaria morbidity but had little effect on vector density (Downs *et al*, 1950 and Moscoso-Carrasco, 1953, as quoted by Gabaldon, 1953a 1953b)

30 *A (M) pulcherrimus* Theobald, 1902 —Vector in Caucasus and Iraq

The females of this species like to concentrate around settlements, but they occur also far from man and his herds. As resting places, they choose buildings as well as outdoor places, burrows, vegetation and the like. They viciously bite man and animals. It is a bold feeder attacking animals and man in the open by day or by night.

Data on its control by the use of insecticides not available

31 *A (M) punctulatus* Donitz, 1901 —Vector in New Guinea, Solomons to Halmahera

Adult females feed and rest indoors or outdoors and take human or cattle blood without much preference.

Data on its control by the use of insecticides not available

32 *A (A) quadrimaculatus* Say, 1924 —Vector in Central, South and East U S A

Adults are most active at night, females fly as far as one mile to obtain animal or human blood meal, and readily enter houses where they often spend daylight hours in dark corners. It is the most abundant anopheline found in houses and other man-made shelters, prefers bovine hosts, but at times or in places feeds on man.

Andrews (1951) recorded reduction in vector density and malaria morbidity in U S A, with D D T residual sprays (200 mg /sq ft)

33 *A (M) rufipes* Gough, 1910 —Vector in West Africa, coastal region

Adults have been found in human dwellings, cowsheds, and outdoor haunts including rock clefts and cavities in banks along streams.

Data on its control by the use of insecticides not available

34 *A (A) sacharovi* Favre, 1903 —It is an important vector in Balkans, Near East, Central Russia and West China

Adults enter human habitations where they persistently bite man. They sometimes feed indiscriminately on man and domestic animals and rest indoors or outdoors.

Reduction or eradication of the vector species and reduction in malaria morbidity has been recorded from Greece (D D T 100 mg /sq ft) (Livadas, 1950), Italy (D D T 200 mg /sq ft) (Missiroli *et al*, 1948) and Jordan (D D T 200 mg /sq ft) (Farid, 1953) with D D T residual sprays.

35 *A (M) sergenti* Theobald, 1907 —Vector in Canary Islands, Egyptian oases, Transjordan and Israel

Adults readily enter houses, and bite most frequently after dark, prefer animal blood but at times bite man. They are found resting in caves, karezes, also in houses and tents.

In Jordan, Farid (1953) observed slight reduction in malaria morbidity but little effect on vector density with D D T applied at the rate of 200 mg/sq ft.

36 *A (M) stephensi mysorensis* Sweet and Rao, 1937—Vector in South India. Considered less important as vector than the type form, but Senior White as quoted by Boyd (1949) considered it to be chief rural carrier in Vizagapatam (India).

This species is less hardy than the type form and has more zoophilic tendencies.

Data on its control by the use of insecticides not available.

37 *A (M) stephensi stephensi* Lisbon, 1901—Vector in Persian Gulf area and India.

It feeds and rests indoors. Adults are commonly found in houses, barracks and cowsheds. Feeds avidly on man.

In West Pakistan, Afridi and Bhana (1947) recorded reduction in vector density and malaria morbidity with D D T sprayed at the rate of 25.38 mg/sq ft. In India similar results were achieved by Adhikari and Ganguli (1949) with D D T applications (100 mg/sq ft).

38 *A (M) subpictus subpictus* Grassi, 1899—Vector in Celebes.

It feeds indoor but may rest indoors or outdoors. Adults are found in large numbers in houses and in cattle sheds. They may feed on man but apparently prefer cattle. Anthropophilic indices as low as zero and as high as 25.0 per cent have been recorded from India.

Data on its control by the use of insecticides not available.

39 *A (M) sundicus* Rodenwaldt, 1926—Vector in North east India, East Pakistan, Indonesia, Andaman Malaya, Sarawak and Borneo.

They rest in houses and cowsheds and are voracious feeders biting by day as well as by night. They may bite indoors or outdoors. In Indonesia it shows an overwhelming preference for human blood even in the presence of cattle. Anthropophilic indices of 94.0 and 86.0 per cent have been recorded from Indonesia.

In India (D D T 100 mg/sq ft) and Indonesia (D D T 200 mg/sq ft) reduction in vector density and malaria morbidity was recorded with D D T residual sprays (Adhikari and Ganguli, 1949 and Van Thiel and Winoto, 1951).

40 *A (M) superpictus* Grassi, 1899—Vector in Eastern Mediterranean countries including southern Italy, Near East, U S S R, and Baluchistan (Pakistan).

Adults readily enter houses, tents and barracks, and females prefer human blood. They are found in large numbers in outside resting places also (caves and karezes). Anthropophilic indices of 48.1, 29.7, and 23.3 per cent of those captured in stables were recorded from Yugoslavia, Greece and Cyprus, respectively.

In Greece, (D D T 180 mg/sq ft), Pakistan (D D T 25.50 mg/sq ft) and Afghanistan with D D T residual sprays (D D T 112.200 mg per sq ft) reduction in vector density and malaria morbidity was recorded (Livadas, 1950, Afridi and Bhana, 1947, Puri and Bhana, 1947, and Rao, 1951).

41 *A (M) varuna* Iyengar, 1924—Vector of local importance in some hilly and foot hill areas of East Central India

The adults are found both in cowsheds and human habitations, and feed readily on man

Senior White (1945) obtained effective control of this species for eight weeks in Jeypore hill tracts, India, with D D T applied at the rate of 50 mg /sq ft

42 *A (A) vestitipennis* Dyar and Knab, 1906—Vector in Mexico and British Honduras

Adult females readily enter houses and feed indoors but may rest in indoor or outdoor shelters They take human or animal blood without much preference

In Mexico with D D T applied at the rate of 200 250 mg per sq ft, Salinas Dopez and Roquet Perez (1950) obtained slight reduction in malaria morbidity but no effect on vector density

GROUP (B)

INDOOR BITERS AND OUTDOOR RESTERS

1 *A (N) albimanus* Wiedemann, 1921—Vector in Central America, West Indies Caribbean Coast, Venezuela, Columbia, Pacific Coast and Ecuador

It feeds indoors but rests in outdoor shelters Adults are nocturnal in habits and avid feeders on man who may be the preferred host, or on horses, cows, goats or pigs They invade houses in large numbers but do not, as a rule, remain in houses after sunrise Its domesticity is low in Venezuela Out of 100 mosquitoes of this species caught, two to five come from houses Anthropophilic index of 34 per cent has been recorded in Venezuela

With D D T residual sprays, reduction in vector density and malaria morbidity has been recorded in Puerto Rico (D D T 150 200 mg /sq ft) (Gahan and Lindquist, 1945), Ecuador (D D T 150 200 mg /sq ft) (Montalvan 1953) Venezuela (D D T 200 mg /sq ft) (Gabaldon, 1953a 1953b) and Panama (D D T 200 mg /sq ft) (Galindo and Gallardo, 1947 as quoted by Gabaldon, 1953a 1953b) In Mexico there was slight reduction in malaria morbidity but little effect on vector density with D D T applied at the rate of 200 250 mg /sq ft

2 *A (M) fluviatilis* James, 1902—Vector in hill and foot hill regions of India

They feed indoors and a significant fraction of population is in outdoor resting places during the day The species seems to be composed of two biological races, one is strongly anthropophilic, while the other feeds almost exclusively on cattle Anthropophilic indices as high as 87.0 per cent and as low as 1.0 per cent have been recorded in India

With D D T residual sprays (50 60 mg /sq ft) reduction in vector density and malaria morbidity has been recorded in India (Ramakrishnan *et al.*, 1948, Vedamanikkam, 1949, Jaswant Singh and Kariappa, 1949, Viswanathan, 1950, and Srivastava and Chakrabarti, 1952)

3 *A (M) letifer* Gater, 1941, Sandosham, 1945—Vector in Malaya. Adults are found in deeply shaded places in jungle and also in houses. It feeds indoors and outdoors but rests in outdoor shelters. It has marked preference for human blood and seldom attacks cattle (Nair, 1947a).

With D D T application at the rate of 100 mg/sq ft, Nair (1947b 1951) recorded reduction in vector density and malaria morbidity.

4 *A (M) leucosphyrus leucosphyrus* Donitz, 1901—Vector in North east India, Borneo, Indonesia and Burma.

Adults are wild and naturally occur in dense jungle, but may be found in houses also. It feeds indoors but rests outdoors. Adults appear to take human blood without much preference. Anthropophilic index of 75.5 per cent has been recorded in India.

Data on its control by the use of insecticides not available.

5 *A (M) maculatus maculatus* Theobald, 1901—Vectors in Malaya, Siam, Yunnan and Hong Kong.

Adults enter houses readily, bite man between 9 p.m. and 2 a.m. and during the day are found in houses, cattle sheds and outdoor resting places. Apparently feeding habits of this species differ in different parts. In Assam, Indo China, Siam, China and Philippines it appears to be zoophilic while in Malaya and Siam it is anthropophilic. Anthropophilic indices as high as 97.0 and as low as 2.8 per cent have been recorded in Indonesia and Philippines, respectively.

Schiphorst (1952) (as quoted by Gabaldon 1953a 1953b), obtained reduction in malaria morbidity with D D T residual application (200 mg/sq ft) whereas Wallace (1948) recorded reduction in vector density with little effect on malaria morbidity with D D T applied at the rate of 100 mg/sq ft.

6 *A (M) minimus flavescens* Ludlow 1914—Vector in Philippines, Siam, Java and Celebes.

It bites indoors but rests in outdoor shelters. Adults bite man and cattle without much discrimination. They enter houses at night to feed but do not rest during the day, they frequently rest under overhanging stream banks.

In Philippines Smith and Dy (1949) obtained little effect on vector density with D D T applied at the rate of 200 mg per sq ft. Bhatia (1953) (as quoted by Pant Singh *et al.*, 1954) recorded reduction in vector density and malaria morbidity with D D T residual spray applied at the rate of 200 mg per sq ft.

7 *A (A) novumbrus* Strickland, 1916—Vector in Malaya.

It may feed indoors or outdoors but it rests in outdoor shelters. There is sufficient evidence regarding its preference for human or cattle blood.

Data on its control by the use of insecticides not available.

8 *A (M) pharoensis* Theobald, 1901—Vector in Egyptian delta and oases, Uganda, Congo.

It feeds indoors but rests in outdoor shelters. It may be strongly (South Africa) or weakly (Kenya) anthropophilic. In Egypt, anthropophilic index of

those caught from houses and tents was 97.5 per cent and those from stables 10.8 per cent. Apparently spends the day in ricefields as none are found in stables, houses or similar shelters (Nile Valley). Prof G. Macdonald's experience is very much against this observation (personal communication, 1954).

Data on its control by the use of insecticides not available

9 *A. (A.) punctumaculatus* Dyar and Knab, 1906 — Vector in Columbia, Peru and Panama

It feeds and rests indoors and outdoors and prefers cattle blood. Adults are abundant in undrained jungle areas and the females engage in flights, invade dwellings and feed on human blood.

Data on its control by the use of insecticides not available

10 *A. (A.) umbrosus* Theobald, 1903 — Vector in Malaya and Indonesia

It feeds indoors or outdoors but rests outdoors. Adults are fierce biters and are found in deeply shaded places in dense forests and also in houses. They have marked preference for human blood. Anthropophilic index of 95.0 per cent has been recorded from Malaya.

Data on its control by the use of insecticides not available

GROUPS (C) AND (D)

OUTDOOR BITERS AND INDOOR RESTERS, OUTDOOR BITERS AND OUTDOOR RESTERS

1 *A. (A.) bancrofti bancrofti* Giles, 1902 — Vector in Australia and Dutch New Guinea

Adults rarely frequent houses. It is said to vary a great deal in its feeding habits in different areas. In South Queensland it attacks human beings in the bush in the daytime while at Cairns it is said to show some definite discrimination against man.

Data on its control by the use of insecticides not available

2 *A. (A.) barbirostris* Vander Wulp, 1884 — Vector in Malaya and Indonesia

To a large extent this is a wild species. It is more frequently found in houses in the Indian areas than further east. It is the common species in houses in Celebes. The form occurring in India seems to prefer blood of domestic animals, but in Celebes this species is apparently anthropophilic. Anthropophilic index of 9.0 (cattle present) and 31.0 (cattle scarce) per cent have been recorded from Indonesia and 95 per cent from Malaya.

Data on its control by the use of insecticides not available

3 *A. (K.) bellator* Dyar and Knab, 1906 — Vector in Brazil and Trinidad

It may feed indoors or outdoors but rests in outdoor shelters. In Trinidad it does not enter houses in numbers and transmission of malaria is undoubtedly almost entirely out of doors. It prefers animal blood but may feed on man.

In Brazil, Pinotti (1951) recorded reduction in malaria morbidity but little effect on vector density with DDT applied at the rate of 200 mg/sq ft.

4 *A (M) hargreavesi* Evans, 1927—Vector in West Africa inland
It feeds outdoors but may rest in indoor or outdoor shelters Takes human or animal blood without much preference
Data on its control by the use of insecticides not available

5 *A (A) hyrcanus nigerrimus* Giles, 1900—Vector in Indo-China, Malaya and Indonesia
Adults are rarely found in houses but are found more often in cattlesheds They feed and rest outdoors They bite man outside in the evening and even in the shade during the day This is considered to be a zoophilic species Anthro-
pophilic indices of 83.0, 30.2, and 3.8 per cent have been recorded from Indonesia
Malaya and India, respectively

Data on its control by the use of insecticides not available
6 *A (A) hyrcanus williamsoni* Baisas and Hu, 1936—Vector in Java and Celebes
It feeds and rests indoors or outdoors There is insufficient evidence regarding its preference for human or cattle blood
Data on its control by the use of insecticides not available

7 *A (N) nuneztovari* Gabaldon, 1940—Vector in Venezuela
Authentic data on its habits not available
Gabaldon (1953a, 1953b) with DDT application (200 mg/sq ft) in Venezuela, obtained slight reduction in malaria morbidity but little effect on vector density

8 *A (M) tessellatus* Theobald, 1901—Vector in Maldiv islands
Adults are found resting among trees in the jungle along banks of streams, but have been taken also in houses and cowsheds
Data on its control by the use of insecticides not available

SUMMARY

The observations on malaria control *vis-a-vis* the application of insecticides has been reviewed from the global standpoint
(a) Use of residual insecticides has resulted in effective control of malaria transmitted by the following vector species

A. aconitus, *A. albipennis*, *A. annularis*, *A. aquasalis*, *A. atroparvus*, *A. aztecus*, *A. claviger*, *A. cruzi*, *A. culicifacies*, *A. darlingi*, *A. farauti*, *A. frederborni*, *A. funestus*, *A. gambie*, *A. hyrcanus sinensis*, *A. labbranchie*, *A. maculipennis*, *A. maculipennis*, *A. mangynus*, *A. messe*, *A. philippinensis*, *A. pseudopunctipennis*, *A. quadrimaculatus*, *A. sacharovi*, *A. stephensi*, *A. sundanicus*, *A. albimanus*, *A. fluvialis*, *A. letifer*, *A. maculatus* and *A. minimus minimus*

(b) In some countries, use of residual insecticides has not resulted in effective control of malaria in respect of the following vector species due to the various factors outlined

(c) It may, however, be pointed out that in spite of the fact that insecticides have been used for the control of malaria for about ten years there are a number of species listed below about which no data is available

A. pulcherrimus, *A. gambiæ melas*, *A. hancocki*, *A. hargreavesi*, *A. moucheti nigeriensis*, *A. pharoensis*, *A. rufipes*, *A. barbirostris*, *A. hyrcanus nigerrimus*, *A. jeyporiensis candidiensis*, *A. leucosphyrus leucosphyrus*, *A. novumbrosus*, *A. stephensi mysorensis*, *A. subpictus subpictus*, *A. umbrosus*, *A. bancrofti bancrofti*, *A. punctulatus*, *A. kochi*, *A. punctimaculatus*, *A. brunneipes*, *A. funestus emeriensis*, *A. nili*, *A. hyrcanus williamsoni*, *A. ludlowi torakala* and *A. tessellatus*.

REFERENCES

- A. L. J. 3, pp 1-37
 Ibid 1, pp 79-87
 South African J Sci May pp 289-290
 J Nat Mal Soc, 10 pp 99-113
 nd
 Trans Roy Soc Trop Med Hyg 40, pp 809-820
 Malarology—A comprehensive survey of all aspects of
 BERTRAM D M (1951)
 COVELL G (1927)
 Idem (1931)
 CSEH FORTES S (1950)
 DOWLING M A C (1951)
 DOWNS W G and BORDAS E (1951)
 DOWNS W G, CELLIS, H and GAHAN J B
 (1950)
 FARID M A (1953)
 FLOCH H (1952)
 GABALDON A (1953a)
 Idem (1953b)
 GABALDON A and BERTI A L (1954)
 GAHAN J B and LINDQUIST A W (1945)
 GILLETTE H (1953)
 GILROY A B (1951)
 HACKETT L W (1950)
 HAJRA B N (1948)
 JADIN J (1951)
 Rec Mal Surt Ind 2 pp 1-48
 Doc Med Geogr et Trop 4 pp 117-133
 Bull World Health Org 4, pp 443-461
 J Nat Mal Soc 10, pp 350-358
 Amer J Hyg 52, pp 348-350
 Paper World Health Org J Mal 80
 Arch Inst Pasteur de la Guyane Francaise et du terr
 de l'Inde ne Publ 1951
 Paper presented at the 5th International Congress on
 Tropical Medicine and Malaria Istanbul Turkey
 Rev de Mal 32 pp 150-171
 Amer J Trop Med Hyg 3 pp 793-807
 J Econ Ent 38, pp 1-30
 Annual report of the Malaria Division Health Depart
 ment Trinidad and Tobago Monograph
 pp 1-70
 Ind J Mal 5, pp 171-182
 Bull Nat Soc Ind Mal Mosq Dis 2, pp 31-40
 Ind J Mal 3 pp 1-11
 Ibid 3 pp 285-305
 Bull Nat Soc Ind Mal Mosq Dis 2, pp 31-40
 Ind J Mal 5 pp 235-250
 Ibid 4 pp 385-397
 Ibid 6, pp 117-122
 Rev de Mal 29 pp 73-80
 Rend Inst Sup San to 11, pp 759-90
 JASWANT SINGH PAL R and SHARMA M I D
 (1951)
 KAR P K (1950)
 KRISHNASWAMI A K. (1952)
 LIVADAS G (1950)
 MISSIROLI A, MOSNA, E and ALESSANDRINI
 M (1948)

- MOYALVAY, J. A. (1957)
 NABH, C. P. (1947a)
 Idem (1947b)
 Idem (1951)
 NAKH-UD-DIN M. (1952)
 PAMPANA, E. J. (1951)
 PIVOTTI, M. (1951)
 PURI, I. M. and BHATIA, M. L. (1947)
 PURI, I. M. and KRISHNAYASWAMI, A. K. (1947)
 RAJENDRAM, S. and JAYEWICKREME, S. R. (1951)
 RAMAKRISHNAN, S. P., KRISHNAN K. S. and RAMAKRISHNAN, V. (1948)
 RAO T. RAMACHANDRA (1951)
 REID, J. A. (1951)
 RAYIFO, S. and DE ZILUETA J. (1952)
 RUSSELL, P. F. (1952a)
 Idem (1952b)
 RUSSELL P. F., LUTHER, S. W. and MAXWELL, R. D. (1946)
 RUSSELL P. F., ROZEBOOM L. E. and STOVE, A. (1943)
 SALINAS DOPEZ and ROQUET PEREZ Z. (1950)
 SENIOR WHITE, R. (1945)
 Idem (1951)
 SIMMONS S. W. and UPHOLT W. M. (1951)
 SMITH, H. F. and DY F. J. (1949)
 SRINIVASTAVA R. S. and CHAKRAVARTI, A. K. (1952)
 VAY GOOR, W. T. and LODENS J. G. (1952)
 VAY TIEL, P. H. and WYNOTE R. M. P. (1951)
 VEDAMANNICKAM J. C. (1949)
 VINCKE, I. H.
 VINAYANATHAN, D. K. (1950)
 WALLACE R. B. (1948)
 WUST, H. R. (1947)
 MS East National de Hygiene Leo Poldo Iguala
 Priv. Guaya QUN, pp 1-53
 Med J Malaya, 2, pp 165-172
 Ibid. 2, pp 83-124
 Nature, Jan. 13, pp 74-75
 Pakistan J Health 2, pp 21-24
 Bull World Health Org 3, pp 657-619
 J Nat Med Soc, 20, pp 182-183
 Ind J Mal 2, pp 123-191
 Ibid. 2, pp 159-181
 Ibid. 3, pp 73-124
 Ibid. 2, pp 247-282
 Bull World Health Org 3, pp 639-661
 Nature Nov 17 pp 863-865
 Amer J Trop Med Hyg 2, pp 598-611
 Amer J Trop Med Hyg 2, pp 111-123
 Malaria—Basic principles briefly stated Blackwell
 Scientific Publications Oxford
 Practical Malariaology W B Saunders Co
 Philadelphia and London
 Keys to the anopheline mosquitoes of the world Academi
 of National Sciences Philadelphia
 Tobacco Rev Patu G Med Trop 2, pp 23-24
 J Mal Inst Ind 6, pp 83-93
 Ind J Mal 5, pp 465-512
 Bull World Health Org 3, pp 53-55
 Acta Medica Philippina 6, pp 81-96
 Ind J Mal 6, pp 381-394
 Doc Med Geogr et Trop 4, pp 144-148
 Abstract in Trop Dis Bull 49, p 930
 Doc Med et Ind Med Trop 3, pp 29-319
 Ind J Mal 3, pp 371-373
 Monograph pp 11-19
 Service Provincial de
 Hygiene Publ que en Katanga Elizabethville
 Malaria and its control in Bombay State Chittrachala
 Press Poona
 Med J Malaya 3, pp 5-37
 J Econ Ent 40, pp 762

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